UNIVERSITEIT GENT

FACULTEIT PSYCHOLOGIE EN PEDAGOGISCHE WETENSCHAPPEN

THE INFLUENCE OF MIMICRY ON EMPATHY FOR PAIN

Lize De Coster

Promotor: Prof. Dr. Marcel Brass
Copromotor: Prof. Dr. Liesbet Goubert

Proefschrift ingediend tot het behalen van de academische graad
van Doctor in de Psychologie

2014

A little sweat ain't never hurt nobody
(Beyoncé Knowles)

CONTENTS

ACKNOWLEDGEMENTS

People to thank. There are so many Others who have meant the world to my Self over the past four years. It will be short. I've always been a girl of few words, especially when my emotions get the better of me. Know that there is a lot more I want to say.

First and foremost, I would like to thank my promoter, Prof. dr. **Marcel** Brass. I have never been good at expressing myself around you, but I hope you know that I would not have wanted to trade my PhD for any other, primarily because you were my supervisor. To me, you encompass the wisdom of a genius researcher with the humility of a great human being. I have been nothing but lucky the past four years, inspired by your critical thinking, great mind, kind help, and never-ending positivity. Thank you.

I would also like to thank Prof. dr. **Liesbet** Goubert and the **pain group** we belong to. Thank you for always being available and willing to help, and not taking the moments of silence from my side against me. I'm indebted to you for showing me new insights and always inspiring alternative ways of thinking.

Other collaborators I would like to thank are Prof. dr. **Michael** Andres, with whom I conducted a brilliant study (in our humble opinion). Being around you made me feel like a better researcher, something I rarely experienced over the past four years. You are kind, patient, and a genius. Prof. dr. **Bruno** Verschuere. We go back to when I was still a student, and you were indispensable in setting up this whole project. The same goes for Prof. dr. **Simone** Kühn. I cannot but look up to you in wonder and be inspired. Prof. dr. **Roeljan** Wiersema. What a great, cool man you are. You made our study so much fun. Prof. dr. **Sven** Müller. All of the effort was

worth it, and I would like to thank you for never giving up. dr. **Charlotte** Desmet and dr. **Jelle** Demanet. Two excellent researchers and beautiful human beings. It was a genuine pleasure to be able to work with you. Prof. dr. **Claus** Lamm. Thank you for your indispensable guidance and critical review of my work. I hope we can work together some time. I would also like to thank my master students, from whom I learned so much. I was incredibly lucky with all of you. **Febe**, **Eleonore**, and **David**. **Emiel**, we will hear a lot from you. And a special shout-out to **Lien**, who has become a dear partner in crime.

My office mates. **Lara**, I cannot explain what you have meant to me since you moved here. You remind me of the kind of person I want to be every day. You made me feel better when I was at my worst, and I love you with a fiery heart. Marry me some day. **Eliane**, my unlikely and dear friend. We have always been an unusual pair but for reasons unexplained we work so well together. I never want to lose sight of you. There is a lot more I want to say, but you know me. I'll tell you at an inappropriate moment.

Zachary, thank you for being confusing. For the beats. Come with me to New York. **Eliana**, we shared a four year journey and I'm happy we are still here together. **Maggie** (you are one of the sweetest persons I know), **Oliver** (you are one of the most positive persons I know), **Chiara** (you are only Mini in size), **Evelyne** (what would I have done without you), **Roma**, **Mario**, **William**, **Paul**, **Carsten**, **Saskia**, **Patricia**.

Thank you to all members of the **Experimental Department**. There are so many of you who helped me, were kind to me, and I will never forget. **Christophe**, we should have met up in Ieper much sooner. **Lies**, I cannot imagine any other secretary.

Marieke. My dearest friend for a long time. We shared so much. I learned from the difficult moments and cherish the beautiful ones. We will

find each other again. **Kristien**. You have one of the kindest hearts and most elegant souls I know. You encompass everything I aspire to be in live.

3G! Many have come and gone (**Ines**, **Stefanie**). **Rosie**, thank you for being so incredibly kind and for sharing the ups and downs with me. **Anke**, one day it'll happen for us too. **Miguel** and **Alex** in Berlin. Best time of my life thanks to you.

All the dancers I shared movements with. Special thanks to **Jannick**, my oldest friend and most reliable dance partner. **Joris**, thank you for not giving up on inviting me. **Lien**, **Anna**, **Sophie**. Let's go viral one day.

My **family**. My **parents**. My loving, cool, crazy parents. I think it's no coincidence you have raised three beautiful, independent daughters. You won't hear me say this often: you did a marvelous job. You always supported me, made me feel like I could do anything I wanted, and loved me throughout all my difficult moments. Thank you thank you thank you.

Last but not least, I want to thank the two most important Others in my life: my sisters **Margot** and **Freya**. My soul mates, my better Selves. I would be nothing without you, and I am everything thanks to you. There is no-one who I love more in this world. You know who I am and still stay with me. I wish this kind of love upon everyone.

Forgive me if I have forgotten anyone, and know that I thank you from the bottom of my heart.

Thank you **all** for providing me with the most important things in life: honesty, respect, and dancing.

CHAPTER 1
INTRODUCTION

"…; and that, not because he's handsome, Nelly, but because he's more myself than I am. Whatever our souls are made of, his and mine are the same,…"

Emily Brontë, Wuthering Heights (p.121)

Credited with creating an intimate form of media communication, Oprah Winfrey is thought to be the Queen of talk show hosts. Seemingly effortless, she is able to get her guests to share their most private details, and provoke exclusive confessions (see Lance Armstrong, 2013). But why does Oprah reign supreme? Figure 1 might provide a first insight, showing clearly how Oprah imitates her guests' posture and mannerisms during interviews. Whether deliberately or not, this imitation mechanism might be crucial to her interview skills…

Figure 1: Oprah at work.

BEING IMITATED AND PROSOCIAL BEHAVIOUR

Imitation is an important part of our everyday life; taking place everywhere, anytime, with anyone (Brass, Bekkering, Wöhlschlager, & Prinz, 2000; Brass, Bekkering, & Prinz, 2001; Chartrand & Bargh, 1999; Lakin & Chartrand, 2003). An important question, however, is why people tend to imitate each other? Chartrand and Bargh (1999) have shown that mimicry (unconscious, automatic imitation) changes the way we experience others. They demonstrated that we like someone who imitates us more, and that the interaction with this person runs more smoothly (Chameleon effect). Since then, a compelling range of social-psychological research has shown that being imitated enhances positive social behaviour towards others (e.g. Kühn et al., 2010; Lakin, Chartrand, & Arkin, 2008; Stel, van Baaren, & Vonk, 2008). van Baaren, Holland, Kawakami, and van Knippenberg (2004), for example, have shown that subjects whose behaviour was mimicked by a confederate were more helpful and generous towards this mimicker. Moreover, they were able to demonstrate that this positive behaviour was not limited to the initial interaction partner but generalized to other people not involved in the interaction, suggesting that mimicry leads to a general prosocial orientation. Other studies demonstrating positive social behaviour as a consequence of imitation have shown that synchronization of movements during dyads leads to more attention for one's interaction partner and a smooth information transfer (Macrae, Duffy, Miles, & Lawrence, 2008), that consumption behaviour can be influenced by imitation (Tanner, Ferraro, Chartrand, Bettman, & van Baaren, 2008), that negotations are facilitated by strategic behavioural imitation (Maddux, Mullen, & Galinsky, 2008), that people with a need for affiliation tend to imitate more (Lakin & Chartrand, 2003), and that prosocial consequences of imitation are also

present during interactions with artificial intelligence partners (Bailenson & Yee, 2005). Kühn et al. (2010) suggest that positive social consequences of being imitated are associated with activation in regions related to reward and emotion (medial orbitofrontal cortex and ventromedial prefrontal cortex). Furthermore, research by Ashton-James, van Baaren, Chartrand, Decety, and Karremans (2007) tried to find an answer to the question why prosocial effects of unconscious imitation are transferred outside of the initial dyadic interaction between mimicker and mimickee. They suggest that being imitated during social interactions leads to a shift towards interdependent and other-oriented self construal. According to these authors, interpersonal imitation enhances self perception of interdependent intimacy with non-specified others and reduces the physical closeness to them, mediating the effect on positive social behaviour. Finally, Stel et al. (2008) have demonstrated that a similar prosocial orientation is elicited in the imitator. They posit that automatic imitation creates affective empathic representations which lead to positive social behaviour towards others, suggesting that affective empathy modulates the effect of imitation on prosocial behaviour.

Thus, imitative behaviour seems to be an essential process by which relationships between people are enhanced. This is important, since tight bonds between humans have been shown to have several (evolutionary) advantages, both on a physical and mental level (Buss & Kendrick, 1998; Chou, Liang, & Sareen, 2011).

EMPATHY FOR PAIN

In their seminal study, Singer et al. (2004) showed for the first time that observing someone else in pain activates pain-related brain regions in

the observer that are also active when directly experiencing pain (empathy for pain). More specifically, several studies have indicated that the affective-motivational dimensions of pain become active when perceiving another person in pain (Goubert, Vervoort, & Craig, 2012; Jackson, Meltzoff, & Decety, 2005; Lamm, Decety, & Singer, 2011; Singer et al., 2006), and that this effect is stronger when having an affective relationship with the person observed (Cheng, Chen, Lin, Chou, & Decety, 2010; Singer et al., 2004). However, although a meta-analysis by Lamm et al. (2011) suggests that the anterior insula (AI) and anterior cingulate cortex (ACC) are most consistently activated during empathy for pain, research has shown that the sensory dimension of pain becomes active as well (Bufalari, Aprile, Avenanti, Di Russo, & Aglioti, 2007; Cheng, Yang, Lin, Lee, & Decety, 2008; Lamm, Nusbaum, Meltzoff, & Decety, 2007; Loggia, Mogil, & Bushnell, 2008; for a review see Keysers, Kaas, & Gazzola, 2010). Furthermore, Singer et al. (2004) suggest that these reactions serve an important function since they are the basis for our ability to form subjective representations of others' feelings, allowing us to understand the emotional value of stimuli for others and predict the consequences. Since being imitated has been demonstrated to have several positive social consequences, we wanted to investigate whether it also influences observing another person in pain. Several studies have already indicated that empathy for pain can be modulated by both cognitive top-down (e.g. Cheng et al., 2007; Decety, Echols, & Corell, 2009; de Vignemont & Singer, 2006; Hein & Singer, 2008; Lamm, Meltzoff, & Decety, 2010; Singer et al., 2006), and bottom-up features (e.g. Han, Fan, & Mao, 2008; Xu, Zuo, Wang, & Han, 2009; Yang, Decety, Lee, Chen, & Cheng, 2009). The influence of being imitated on empathy for pain, however, had never been the subject of research.

The aim of the current thesis was thus to investigate whether being imitated can modulate responses to observing someone else in pain. Since being imitated increases prosocial behaviour (e.g. Kühn et al., 2010; Lakin et al., 2008; van Baaren et al., 2004), it seems intuitive that it would increase reactions to observing others in pain. Furthermore, we wanted to investigate which mechanism(s) combine(s) both research domains, by examining which process mediates the interaction of motor imitation on empathy for pain. More specifically, we aimed to explore whether a shared representational account could be used to explain the effect of being imitated on empathy for pain, since both have been separately linked to this idea (Brass & Heyes, 2005; Bastiaansen, Thioux, & Keysers, 2009; Heberlein & Atkinson, 2009). Thus, we predicted that being imitated would increase self-other confusion due to a common coding of own and others' actions (e.g. Brass, Derrfuss, Cramon, & von Cramon, 2003; Liepelt, von Cramon, & Brass, 2008), enhancing reactions to observing someone else in pain.

In order to investigate whether being imitated has an influence on empathy for pain, we developed a paradigm that combined literature on being imitated and empathy for pain. In this paradigm, individuals sit in front of a computer screen placing their right hand on a custom-built response box that is able to detect lifting movements. Simultaneously, a right hand on screen is observed, in exactly the same position. The task for subjects is then to randomly and voluntarily lift one of four fingers, namely the index, middle, ring, or little finger. Subsequently, the hand on screen either immediately imitates these movements (being imitated condition) or not (not being imitated condition). After approximately 20 of these movements (all imitation or all non-imitation), the hand on screen receives painful stimulation. For this purpose, we had professionals develop ten different movies in which it is observed how painful stimulation is applied to

a right hand (*'bore goes into the hand'*, *'hammer is smacked on the hand'*, *'hot iron is pressed on the hand'*, *'knife cuts the hand'*, *'nail is knocked into the hand'*, *'nail of the ring finger is pulled out of the hand'*, *'paper makes a paper cut in the hand'*, *'pincers pinches the hand'*, *'sandpaper is rubbed over the hand'*, *'stapler puts a staple into the hand'*; see Figure 2 for an example). During and after these pain movies, it was possible to measure reactions to observing the painful stimulation and we could verify whether these reactions were stronger after being imitated compared to not being imitated.

Figure 2: Picture of the bore pain movie, in which a bore goes into the back of the hand.

OUTLINE OF THE DISSERTATION

In a series of studies, we applied this paradigm to explore the hypothesis that being imitated increases empathy for pain. In a first behavioural study, we used self-reports and psychophysiological responses to look at reactions when observing a hand in pain. This study established our paradigm as a valuable tool to investigate our research question, and provided first evidence for the idea that being imitated influences empathy

for pain due to increased self-other overlap. In a second study, we measured motor evoked potentials (MEPs) via transcranial magnetic stimulation (TMS), exploring whether being imitated also affects action tendencies when observing someone else in pain. Third, in a functional magnetic resonance imaging (fMRI) study, we were able to look directly at brain activation during pain perception, comparing conditions in which participants were being imitated or not. Finally, we performed a patient study with adults with high functioning autism (HFA) using the paradigm to compare the modulation of empathy for pain by being imitated in adults with HFA and typically developing (TD) adults.

In **Chapter 2**, we describe a study in which we used the aforementioned paradigm to investigate whether being imitated leads to higher empathy for pain. Since it was important to explore the validity of the paradigm, we focused on explicit and implicit indirect measures of empathy for pain. First, we used a self-report measure after each pain movie, questioning subjects' feelings regarding the other person's pain and own experienced pain, combined with unpleasantness (affective) and intensity (sensory) judgements. In addition, we measured psychophysiological responses such as the startle blink reflex, skin conductance, and heart rate changes. All measures were seen as indices of autonomic functioning that have been shown to be responsive to negative emotional stimuli (Bradley, Codispoti, Cuthbert, & Lang, 2001; Vrana, Spence, & Lang, 1988). In a first experiment, we aimed to investigate whether being imitated increases affective responses to seeing someone else in pain using both explicit and implicit responses. Furthermore, in a second experiment, we wanted to explore whether self-other confusion modulated the effect. By creating a spatial variation of the above described paradigm (tilting the screen and placing participants' hand under it, hidden from their own view), we linked

our setup to rubber hand illusion paradigms, in which subjects feel ownership over a rubber hand when viewing this rubber hand being stroked simultaneously with their own hidden hand (Botvinick & Cohen, 1998). Since this illusion is also thought to reflect sharing of representations between self and other (e.g. Tajadura-Jiminez, Grehl, & Tsakiris, 2012), this second experiment allowed us to explore self-other overlap as an underlying mechanism. Thus, in this study, we aimed to look at the effect of being imitated on affective responses (both explicit and implicit) when observing someone else in pain in two experiments, and verify whether sharing of representations between self and other is (at least in part) responsible for this effect. Furthermore, these experiments allowed us to investigate the suitability and validity of our newly developed paradigm for the first time.

In **Chapter 3**, a study is described in which we performed TMS to look at MEPs of the first dorsal interroseus of the right hand when observing the hand on screen in pain. Using this method, we were able to explore whether action tendencies were affected by our imitation manipulation, providing us with compelling evidence that being imitated influences bodily reactions when observing pain, and supporting the idea that such a manipulation is strongly reflected upon the self. The primary aim of the study, however, arose from a discrepancy in the literature. Several TMS studies have shown that the observation of painful stimulation delivered to the hand of a human model induces a decrease in corticospinal excitability (CSE) in the hand of the observer (e.g. Avenanti, Bueti, Galati, & Aglioti, 2005; Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2006). However, other findings indicate that is decrease is not universal. It has been shown that this inhibition is reduced in individuals with high levels of trait-personal distress (Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2009) and that pain synesthetes (i.e. individuals who experience actual pain when observing

injury to another) show a significant increase in CSE while observing pain in others (Fitzgibbon et al., 2012). In this experiment, we wanted to investigate whether the nature of these CSE modulations are dependent upon the control subjects exert over the observed hand in pain. This TMS study was crucial to gain insight into contradicting findings in the literature concerning reactions of the motor system when observing others in pain. Furthermore, we wanted to explore whether our imitation manipulation was powerful enough to modulate action tendencies.

In **Chapter 4**, we present an fMRI study that was conducted to investigate directly whether being imitated increases pain-related brain activation in the observer when observing someone else in pain. Specifically, this study allowed us to explore which part of the pain matrix is modulated by the imitation manipulation. Since a meta-analysis of Lamm et al. (2011) has shown that the AI and ACC are most consistently activated during empathy for pain, we expected heightened activity to be concentrated in these regions. Second, it was possible to examine whether self-other overlap mediates the effect of being imitated on empathy for pain by investigating whether brain regions associated with self-other distinction (e.g. temporo-parietal junction; Brass, Ruby, & Spengler, 2009; Spengler, von Cramon, & Brass, 2010) were modulated by the imitation manipulation. Thus, this fMRI study allowed us to investigate whether being imitated increases pain-related brain activation when observing someone else in pain. Furthermore, activity in regions related to self-other distinction provided neural support for the idea that increased self-other merging mediates this influence.

In **Chapter 5**, we applied the paradigm to adults with autism spectrum disorder (ASD), more specifically HFA. ASD is a pervasive neurodevelopmental disorder characterized by abnormalities in social communication and interaction and restricted and repetitive patterns of

behaviour, interests, or activities (DSM-5, American Psychiatric Association, 2013). In addition, a large number of studies suggest deficiencies in imitation and empathy abilities. However, the nature of these abnormalities is a hot topic of debate. While imitation was initially thought to be reduced in ASD (for a review see Williams, Whiten, & Singh, 2004), more recent studies have contradicted these findings (see for example Spengler, Bird, & Brass, 2010 for hyperimitation). Second, empathy has been argued to be deficient in adults with ASD as well (Baron-Cohen & Wheelwright, 2004). However, while early research indicated an absence or reduction of empathic responses in ASD (e.g. Minio-Paluello, Baron-Cohen, Avenanti, Walsh, & Aglioti, 2009), more recent research suggests otherwise (e.g. Hadjikhani et al., 2014). With the current paradigm (using the explicit and implicit measures used in the Chapter 2), we were able to further investigate whether people with ASD have problems in being imitated and empathy, and test whether this influence of being imitated on empathy for pain in adults with HFA is similar or different from that of TD adults. This final empirical study provided us with crucial insights into the empathic abilities of ASD, and the influence of being imitated on these empathic responses.

Finally, in the **General Discussion**, we summarize across all chapters and give an overview of strengths and limitations of the current thesis, and provide directions for future research.

REFERENCES

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Ashton-James, C., van Baaren, R. B., Chartrand, T. L., Decety, J., & Karremans, J. (2007). Mimicry and me: The impact of mimicry on self-construal. *Social Cognition, 25,* 518-535. doi : 10.1521/soco.2007.25.4.518

Avenanti, A., Bueti, D., Galati, D., & Aglioti, S. M. (2005). Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nature Neuroscience, 8,* 955-960. doi: 10.1038/m1481

Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2006). Stimulus-driven modulation of motor-evoked potentials during observation of others' pain. *Neuroimage, 32*, 316-324. doi: 10.1016/j.cortex.2008.10.004

Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2009). The pain of a model in the personality of an onlooker: Influence of state-reactivity and personality traits on embodied empathy for pain. *Neuroimage, 44*, 275-283. doi: 10.1016/j.neuroimage.2008.08.001

Bailenson, J. N., & Yee, N. (2005). Digital Chameleons – Automatic assimilation of nonverbal gestures in immersive virtual environments. *Psychological Science, 16,* 814-819. doi: 10.1111/j.1467-9280.2005.01619.x

Baron-Cohen, S., & Wheelwright, S. (2004). The empathy quotient: an investigation of adults with Asperger syndrome or high functioning, and normal sex differences. *Journal of Autism and Developmental Disorders, 34,* 163-175. doi: 10.1023/B:JADD.0000022607.19833.00

Bastiaansen, J. A. C. J. Thioux, M., & Keysers, C. (2009). Evidence for mirror systems in emotions. *Philosophical Transactions of the Royal Society B – Biological Sciences, 364,* 2391-2404. doi: 10.1098/rstb.2009.0058

Botvinick, M., & Cohen, J. (1998). Rubber hands 'feel' touch that eyes see. *Nature, 391*, 756-756. doi:10.1038/35784

Bradley, M. M., Codispoti, M., Cuthbert, B. N., & Lang, P. J. (2001). Emotion and motivation I: Defensive and appetitive reactions in picture processing. *Emotion, 1,* 276-298. doi: 10.1037/1528-3542.1.3.276

Brass, M., Bekkering, H., Wohlschläger, A., & Prinz, W. (2000). Compatibility between Observed and Executed Finger Movements: Comparing Symbolic, Spatial, and Imitative Cues. *Brain and Cognition, 44,* 124-143. doi: 10.1006/brcg.2000.1225

Brass, M., Bekkering, H., & Prinz, W. (2001). Movement observation affects movement execution in a simple response task. *Acta Psychologica, 106*, 3-22. doi: 10.1016/S0001-6918(00)00024-X

Brass, M., Derrfuss, J., Cramon, G. M. V., & von Cramon, D. Y. (2003). Imitative response tendencies in patients with frontal brain lesions. *Neuropsychology, 17,* 265-271. doi: 10.1037/0894-4105.17.2.265

Brass, M., & Heyes, C. M. (2005). Imitation: Is cognitive neuroscience solving the correspondence problem? *Trends in Cognitive Science, 9,* 489-495. doi: 10.1016/j.tics.2005.08.007

Brass, M., Ruby, P., & Spengler, S. (2009). Inhibition of imitative behaviour and social cognition. *Philosophical Transactions of the Royal Society B-Biological Sciences, 364*, 2359-2367. doi: 10.1098/rstb.2009.0066

Bufalari, I., Aprile, T., Avenanti, A., Di Russo, F., & Aglioti, S. M. (2007). Empathy for pain and touch in the human somatosensory cortex. *Cerebral Cortex, 17,* 2553-2561. doi: 10.1093/cercor/bh1161

Buss, D. M., & Kenrick, D. T. (1998). Evolutionary social psychology. In D. T. Gilbert, S. T. Fiske, & G. Lindzey (Eds.), *The handbook of social psychology (4th ed., pp. 982-1026).* New York: Oxford University Press.

Chartrand, T. L., & Bargh, J. A. (1999). The Chameleon effect: The perception-behaviour link and social interaction. *Journal of Personality and Social Psychology, 76,* 893-910. doi: 10.1037/0022-3514.76.6.893

Cheng, Y., Lin, C-P., Liu, H-L., Hsu, Y-Y., Lim, K-E., Hung, D., & Decety, J. (2007). Expertise modulates the perception of pain in others. *Current Biology, 17,* 1708-1713. doi: 10.1016/j.cub.2007/09/020

Cheng, Y., Yang, C-Y., Lin, C-P., Lee, P-L., & Decety, J. (2008). The perception of pain in others suppresses somatosensory oscillations: A magnetoencephalography study. *Neuroimage, 40,* 1833-1840. doi: 10.1016/j.neuroimage.2008.01.064

Chou, K. L., Liang, K., & Sareen, J. (2011). The association between social isolation and DSM-IV mood, anxiety, and substance use disorders: wave 2 of the National Epidemiologic Survey on Alcohol and Related Condition. *Journal of Clinical Psychiatry, 72,* 1468-1476. doi: 10.4088/JCP.10m06019gry

Decety, J., Echols, S. C., & Correll, J. (2009). The blame game: the effect of responsibility and social stigma on empathy for pain. *Journal of Cognitive Neuroscience, 22,* 985-997. doi: 10.1162/jocn.2009.21266

de Vignemont, F., & Singer, T. (2006). The emapthic brain: How, when, and why? *Trends in Cognitive Sciences, 10,* 435-441. doi: 10.1016/j.tics.2006.08.008

Fitzgibbon, B. M., Enticott, P. G., Bradshaw, J. L., Giummarra, M. J., Chou, M., Georgiou-Karistianis, N., & Fitzgerald, P. B. (2012). Enhanced corticospinal response to observed pain in pain synesthetes. *Cognitive, Affective, & Behavioral Neuroscience, 12,* 406-418. doi: 10.3758/s13415-011-0080-8

Goubert, L., Vervoort, T., & Craig, K. D. (2012). Empathy and pain. In R. F. Schmidt & G. F. Gebhart (Eds.), *Encyclopedia of Pain, Second Edition.* Heidelberg: Springer-Verlag.

Grezes, J., & Decety, J. (2001). Functional anatomy of execution, mental simulation, observation, and verb generation of actions: A meta-analysis. *Human Brain Mapping, 12,* 1-19. doi: 10.1002/1097-0193(200101)

Hadjikhani, N., Zürcher, N. R., Rogier, O., Hippolyte, L., Lemonnier, E., Ruest, T., Ward, N., Lassalle, A., Gillberg, N., Billstedt, E., Helles, A., Gillberg, C., Solomon, P., Prkachin, K. M., & Gillberg, C. (2014). Emotional contagion for pain is intact in autism spectrum disorders. *Translational Psychiatry (e343).* doi: 10.1038/tp.2013.113

Han, S. H., Fan, Y., & Mao, L. (2008). Gender difference in empathy for pain: an electrophysiological investigation. *Brain Research, 1196,* 85-93. doi: 10.1016/jbrainres.2007.12.062

Heberlein, A. S., & Atkinson, A. P. (2009). Neuroscientific evidence for simulation and shared substrates in emotion recognition. *Emotion Review, 1,* 162-177. doi: 10.1177/1754073908100441

Hein, G., & Singer, T. (2008). I feel how you feel but not always: The empathic brain and its modulation. *Current Opinion in Neurobiology, 18,* 153-158. doi: 10.1016/j.conb.2008.07.012

Jackson, P. L., Meltzoff, A. N., & Decety, J. (2005). How do we perceive the pain of others? A window into the neural processes involved in empathy. *Neuroimage, 24,* 771-779. doi: 10.1016/j.neuroimage.2004.09.006

Keysers, C., Kaas, J. H., & Gazzola, V. (2010). Somatosensation in social perception. *Nature Reviews Neuroscience, 11*, 417-428. doi: 10.1038/nrn2833

Kühn, S., Muller, B. C., van Baaren, R. B., Wietzker, A., Dijksterhuis, A., & Brass, M. (2010). Why do I like you when you behave like me? Neural mechanisms mediating positive consequences of observing someone being imitated. *Social Neuroscience, 5*, 384-392. doi: 10.1080/17470911003633750

Lakin, J. L., & Chartrand, T. L. (2003). Using nonconscious behavioral mimicry to create affiliation and rapport. *Psychological Science, 14,* 334-339. doi: 10.1111/1467-9280.14481

Lakin, J. L., Chartrand, T. L., & Arkin, R. M. (2008). I am too just like you – Nonconscious mimicry as an automatic behavioral response to social exclusion. *Psychological Science, 19*, 816-822. doi: 10.1111/j.1467-9280.2008.02162.x

Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage, 54*, 2492-2502. doi: 10.1016/j.neuroimage.2010.10.014

Lamm, C., Meltzoff, A. N., & Decety, J. (2010). How do we empathize with someone who is not like us? A functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience, 22*, 362-376. doi: 10.1162/jocn.2009.21186

Lamm, C., Nusbaum, H. C., Meltzoff, A. N., & Decety, J. (2007). What are you feeling? Using functional magnetic resonance imaging to assess the modulation of sensory and affective responses during empathy for pain. *PloS One, 12*: e 1292. doi: 10.1371/journal.pone.0001292

Liepelt, R., von Cramon, D. Y., & Brass, M. (2008). What Is Matched in Direct Matching? Intention Attribution Modulates Motor Priming. *Journal of Experimental Psychology: Human Perception and Performance, 34*, 578-591. doi: 10.1037/0096-1523.34.3.578

Loggia, M. L., Mogil, J. S., & Bushnell, M. C. (2008). Empathy hurts: Compassion for another increases both sensory and affective components of pain perception. *Pain, 136*, 168-176. doi: 10.1016/j.pain.2007.07.017

Macrae, C. N., Duffy, O. K., Miles, L. K., & Lawrence, J. (2008). A case for hand waving: Action synchrony and person perception. *Cognition, 109*, 152-156. doi: 10.1016/j.cognition.2008.07.007

Maddux, W. W., Mullen, E., & Galinsky, A. D. (2008). Chameleons bake bigger pies and take bigger pieces: Strategic behavioural mimicry facilitates negotiation outcomes. *Journal of Experimental Social Psychology, 44*, 461-468. doi: 10.1016/j.jesp.2007.02.003

Minio-Paluello, I., Baron-Cohen, S., Avenanti, A., Walsh, V., & Aglioti, S. M. (2009). Absence of embodied empathy during pain observation in Asperger Syndrome. *Biological Psychiatry, 65*, 55-62. doi: 10.1016/j.biopsych.2008.08.006

Singer, T., Seymour, B., O' Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for Pain Involves the Affective but not Sensory Components of Pain. *Science, 303*, 1157-1162. doi: 10.1126/science.1093535

Singer, T., Seymour, B., O' Doherty, J. P., Stephan, K. E., Dolan, R. J., & Frith, C. D. (2006). Empathic neural responses are modulated by the perceived fairness of others. *Nature, 439*, 466-469. doi: 10.1038/nature04271

Spengler, S., Bird, G., & Brass, M. (2010). Hyperimitation of actions is related to reduced understanding of others' minds in autism spectrum conditions. *Biological Psychiatry, 15*, 1148-1155. doi: 10.1016/j.biopsych.2010.09.017

Spengler, S., von Cramon, D. Y., & Brass, M. (2010). Resisting motor mimicry: Control of imitation involves processes central to social cognition in patients with frontal and temporo-parietal lesion. *Social Neuroscience, 19*, 98-106. doi: 10.1080/17470911003687905

Stel, M., van Baaren, R. B., & Vonk, R. (2008). Effects of mimicking: Acting prosocially by being emotionally moved. *European Journal of Social Psychology, 38,* 965-976. doi: 10.1002/ejsp.472

Tajadura-Jimenez, A., Grehl, S., & Tsakiris, M. (2012). The other in me: Interpersonal multisensory stimulation changes the mental representation of the self. *PLOS one, 7*. doi: 10.1371/journal.pone.0040682

Tanner, R. J., Ferraro, R., Chartrand, T. L., Bettman, J. R., & van Baaren, R. (2008). Of Chameleons and Consumption: The Impact of Mimicry on Choice and Preferences. *Journal of Consumer Research, 34*, 754-766

van Baaren, R. B., Holland, R. W., Kawakami, K., & van Knippenberg, A. (2004). Mimicry and Prosocial Behavior. *Psychological Science, 15,* 71-74. doi: 10.1111/j.0963-7214.2004.01501012.x

Vrana, S. R., Spence, E. L., & Lang, P. J. (1988). The startle probe response: A new measure of emotion? *Journal of Abnormal Psychology, 97,* 487-491. doi: 10.1037/0021-843X.97.4.487

Williams, J. H. G., Whiten, A., & Singh, T. (2004). A systemic review of action imitation in autism spectrum disorder. *Journal of Autism and Developmental Disorders, 34*, 285-299. doi: 10.1023/B:JADD.0000029551.56735.3a

Xu, X. J., Zuo, X. Y., Wang, X. Y., & Han, S. H. (2009). Do you feel my pain? Racial group membership modulates empathic neural responses. *Journal of Neuroscience, 29*, 8525-8529. doi: 10.1523/JNEUROSC.2418-09.2009

Yang, C. Y., Decety, J., Lee, S. Y., Chen, C. Y., & Cheng, Y. W. (2009). Gender differences in the mu rhythm during empathy for pain: An electroencephalographic study. *Brain Research, 1252*, 176-184. doi: 10.1016/j.brainres.2008.11.062

CHAPTER 2
I SUFFER MORE FROM YOUR PAIN WHEN YOU ACT LIKE ME: BEING IMITATED ENHANCES AFFECTIVE RESPONSES TO SEEING SOMEONE ELSE IN PAIN[1]

Social-psychological research suggests that being imitated changes the way we experience others. We like someone who imitates us more, and the interaction with this person runs more smoothly. Whether being imitated also affects basic social reactions such as empathy for pain is an open question. Empathy for pain refers to the observation that perceiving another person in pain results in pain-related brain activation in the observer. The aim of the present study was to combine both lines of research, and investigate whether being imitated can influence empathy for pain. To this end, we developed an experimental approach combining an imitation task with a pain perception task. Subjective reports as well as physiological responses indicated that being imitated enhances affective responses to seeing someone else in pain. Furthermore, using rubber hand illusion measures, we provide evidence for the role of shared representations in the sensory and motor domain as a core underlying mechanism. In this way, our study integrates social-psychological research on being imitated with cognitive research on empathy for pain. This has broad implications, since imitation plays a crucial role in our daily social interactions, and our study provides insights into a basic cognitive mechanism that might underlie these social situations.

---

[1] De Coster, L., Verschuere, B., Goubert, L., Tsakiris, M., & Brass, M. (2013). I suffer more from your pain when you act like me: Being imitated enhances affective responses to seeing someone else in pain. *Cognitive, Affective, & Behavioral Neuroscience, 13,* 519-532. doi: 10.3758/s13415-013-0168-4

INTRODUCTION

Imitation is an important part of our behavioural repertoire. It sometimes occurs automatically, without intention, and even between complete strangers (Brass, Bekkering, Wöhlschlager, & Prinz, 2000; Brass, Bekkering, & Prinz, 2001; Lakin & Chartrand, 2003). Moreover, an extensive body of social-psychological research has shown that imitation is very important for our social life, by changing the way we experience others. Research on the so-called Chameleon effect suggests that we like someone who imitates us more, and that the interaction with this person runs more smoothly (Chartrand & Bargh, 1999). Furthermore, several experiments indicate that being imitated enhances prosocial orientation (positive social behaviour towards others; Lakin, Chartrand, & Arkin, 2008; Stel, van Baaren, & Vonk, 2008; Kühn et al., 2010).

While the positive consequences of being imitated have been demonstrated for relatively complex social behaviour such as liking and prosocial actions, the question arises whether being imitated also influences more automatic and implicit social processes such as reacting to someone else being in pain. Several studies demonstrate that perceiving another person in pain activates brain regions involved in the affective-motivational dimensions of pain (Goubert, Vervoort, & Craig, in press; Jackson, Meltzoff, & Decety, 2005; Lamm, Decety, & Singer, 2011; Singer et al., 2006), especially when having an affective relationship with the person observed (Cheng, Chen, Lin, Chou, & Decety, 2010; Singer et al., 2004). This finding, called empathy for pain, shows that the observation of pain activates pain-related brain regions in the observer that are also active when directly experiencing pain. Thus, it indicates that first person experience of pain and the observation of pain in others are based on shared neural circuits, with growing evidence for both affective and sensory sharing in empathy for pain responses (Bufalari, Aprile,

Avenanti, Di Russo, & Aglioti, 2007; Cheng, Yang, Lin, Lee, & Decety, 2008; Lamm, Nusbaum, Meltzoff, & Decety, 2007; Loggia, Mogil, & Bushnell, 2008; for a review see Keysers, Kaas, & Gazzola, 2010). Several studies have indicated that this sharing of representations when observing someone else in pain can be influenced by a wide range of cognitive mechanisms and is thus modulated by top-down processing (e.g. Cheng et al., 2007; Decety, Echols, & Corell, 2009; de Vignemont & Singer, 2006; Hein & Singer, 2008; Lamm, Meltzoff, & Decety, 2010; Singer et al., 2006). Furthermore, it has been shown that features such as race (Xu, Zuo, Wang, & Han, 2009) and gender (Han, Fan, & Mao, 2008; Yang, Decety, Lee, Chen, & Cheng, 2009) of the person in pain play a crucial role. Decety and Lamm (2006) therefore suggest a model in which the empathic response can be seen as the intertwined influence of both bottom-up and top-down factors.

The aim of our first experiment was to investigate whether being imitated can also influence affective responses to seeing someone else in pain. In particular, we wanted to investigate whether the functional system that is involved in motor imitation interacts with the system that mediates empathy for pain, and explore the underlying mechanisms. While both systems are related to different neural structures (e.g. Grezes & Decety, 2001; Singer et al., 2004), they are based on a similar functional mechanism. Being imitated, as well as empathy for pain, have been related to shared representations of self and other (Brass & Heyes, 2005; Bastiaansen, Thioux, & Keysers, 2009; Heberlein & Atkinson, 2009). Furthermore, the Chameleon effect has already been linked to empathy (the ability to share the affective experiences of others; Singer & Lamm, 2009), and an underlying shared representational system has been proposed here as well (Chartrand & van Baaren, 2009). We predicted that being imitated would increase empathy for pain compared to not being imitated. To test this hypothesis, we developed an experimental approach combining a

simple imitation task (participants performed finger lifting movements that were imitated by a hand on screen or not) with a pain perception task (painful stimulation was applied to the hand on screen), and investigated whether measures of empathy for pain were higher in the imitative condition. To measure whether being imitated would lead to higher empathy for pain, we focused on explicit and implicit responses. First, we used a self-report measure after each pain movie. In addition, since Preston and de Waal (2002) argue that the activation of brain representations can result in somatic and autonomic responses, we tested whether physiological responding was affected. Thus, as a somatic response, we measured the startle blink reflex with electromyography (EMG), a blink reflex of the eye that is part of an automatic reaction to sudden, intense stimuli (Miller, Patrick, & Levenston, 2002). It has been shown that the amplitude of this blink reflex varies according to changes in affective value, with larger amplitudes for negative and smaller amplitudes for positive compared to neutral situations respectively (Vrana, Spence, & Lang, 1988). If being imitated would lead to higher empathy for pain, we expected the startle blink amplitude to be larger in this condition since observing somebody in pain has a negative affective value.

Furthermore, in a second experiment, we aimed to explore the underlying mechanism(s) in more depth, using a spatial variation of the above described paradigm. More specifically, we wanted to investigate whether self-other confusion might underlie the observed effects, by developing a setup in which this confusion was thought to be enhanced. If self-other confusion modulates the influence of being imitated on empathy for pain, we expected this new setup (specifically aimed at eliciting stronger confusion) to increase this influence.

EXPERIMENT 1

Method

Participants. Twenty right-handed volunteers (M_{age} = 19.61, *SD* = 1.56) participated in the study, all with normal or corrected-to-normal vision. To control for possible sex differences (e.g. Han et al., 2008; Yang et al., 2009), only female volunteers were recruited. They were given course credits in exchange for participation, and provided written consent at the beginning of the experiment. The study was granted ethical approval by the local ethics committee.

Experimental design. Blocks of trials consisted of two phases: an action phase in which movements of the subjects were imitated (imitation block) or not (non-imitation block), and a pain perception phase which immediately followed the action phase. In the pain perception phase, one of nine pain movies was presented (see Table 1). Each pain movie was combined two times with both an imitation and non-imitation block, presenting a startle probe during the pain movies to elicit the startle blink reflex once after each type of block. As such, the experiment consisted of 36 trials in the experiment: each of the nine pain movies was combined with both imitative (imitation and non-imitation) and both startle (startle and no startle) conditions. The content of the pain movie, the block condition, and the startle condition were completely randomized.

Stimuli and apparatus. Stimulus material consisted of three types of 720 x 576 video-clips created by professionals: a hand in a resting position, simple finger movements (for the action phase of the task), and pain videos showing a hand receiving pain stimulation (for the pain perception phase).

In the resting state video clip, a right hand with palm down and fingers slightly spread was shown, equal to the position of the right hand of participants placed on the response box. This video remained on screen in between presentation of the other videos in order to assure continuous observation of a right hand on screen.

During the action phase of the experimental task, participants carried out simple finger movements of the index, middle, ring, or little finger. These finger movements were recorded with a custom-built response device using light sensors. This device allowed us to use finger lifting movements of participants as triggers for the presentation of the appropriate finger movement video. As such, participants immediately observed finger movements of the video-taped hand on screen in response to their own lifting movements. For example, in an imitative block, the lifting of an index finger resulted in the presentation of the index finger lifting video, while the middle, ring, or little finger lifting video was shown in a non-imitative block. All finger movement clips had a total duration of 2000 ms.

Finally, nine pain movies in which painful stimulation was applied to the hand on screen were recorded for the pain perception part of the task (all with a total duration of 8000 ms; see Table 1).

Table 1: Description of the different pain movies used in the experiment.

Movie	Description
Bore	Bore goes into the hand
Hammer	Hammer is smacked on the hand
Iron	Hot iron is pressed on the hand
Nail	Nail is knocked into the hand with a hammer
Nail out	Nail of the ring finger is pulled out of the hand
Paper cut	Paper makes a paper cut in the hand
Pincers	Pincers pinch the hand
Sandpaper	Sandpaper is rubbed over the hand
Stapler	Stapler puts a staple into the hand

Self-report measures. During the experiment, four behavioural questions were presented after each pain movie, to measure explicit reactions to observing the hand in pain: *'How unpleasant do you think the other person found the pain stimulation?', 'How intense do you think the other person experienced painful sensations?', 'How unpleasant did you find the pain stimulation yourself?', 'How intense did you experience painful sensations yourself?'.* The first two questions refer to painful experiences of the other person, while the last two questions refer to first person experiences. Both affective (unpleasantness) and sensory (intensity) dimensions of pain had to be rated on a scale from -5 (*not unpleasant/intense at all*) to +5 (*very unpleasant/intense*), since research suggests that both dimensions might be activated when observing someone else in pain (Bufalari et al., 2007; Cheng et al., 2008; Lamm et al., 2007; Loggia et al., 2008; Keysers et al., 2010).

After the experiment, participants filled in the Interpersonal Reactivity Index (IRI; Davis, 1980; for Dutch translation see De Corte et al., 2007) as a

measure of dispositional trait empathy. This questionnaire consists of 28 items which have to be rated on a 5-point Likert scale, and can be divided into four subscales: Perspective Taking, Empathic Concern, Fantasy, and Personal Distress. Internal consistency and construct validity of the Dutch translation suggest that the IRI is a valuable tool to measure self-report empathic tendencies (De Corte et al., 2007). Cronbach's α in the current study for Perspective taking was .62, for Empathic Concern .61, for Fantasy .80, and for Personal Distress .80.

Procedure. Participants were seated in front of a standard computer screen at arm length, and asked to place the four fingers of their right hand on a custom-made response box. As soon as the video-taped right hand appeared on screen (resting state movie), subjects were instructed to voluntary and randomly lift one of their four fingers that was placed on the response box. Immediately after movement of one of the subjects' fingers (delay = 0 ms, estimate of intrinsic delay of computer/software = 66.93 ms), a movie was shown in which the hand on screen performed the same or a different movement for imitation and non-imitation blocks respectively (see Figure 1). After twenty of such movements (all imitative or all non-imitative), one of the pain movies in which the hand on screen receives painful stimulation was immediately presented. After this pain movie, four behavioural questions appeared on screen, which had to be rated on a scale from -5 to +5.

During the pain clips, a burst of white noise of 95 dB(A) was presented after 4000 ms via headphones in only 50 % of the cases in order to avoid predictability of the occurrence of this startle probe (Hawk & Cook, 2000). Prior to the start of the experiment, the startle noise was presented successively five times, in order to control for initial habituation.

Before the start of the experiment, two practice blocks (one of each imitative condition) were presented in order to familiarize subjects with the

procedure. The pain movie shown in these practice blocks was not used in the experimental phase. Furthermore, in these practice blocks, it was verified whether participants understood the behavioural questions correctly. More specifically, they were explicitly made aware of the distinction between other- and self-related questions, and of the fact that the question 'How intense did you experience painful sensations yourself?' related to self-experienced painful sensations alone. Finally, at the end of the experiment, participants filled in the IRI as a measure of trait empathy.

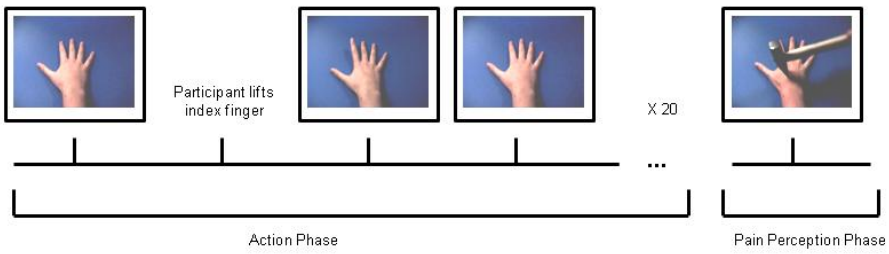


Figure 1: Example of an imitation block in which the participants chooses to lift his/her index finger as a first movement (action phase) and the hammer pain video is shown after 20 movements (pain perception phase).

Electrophysiological recording and analyses. Psychophysiological signals were registered with a Biopac MP150 System and digitalized using AC1001 – AcqKnowledge Software for Windows with Electronic Manual (Biopac Systems, Inc.).

***Startle blink reflex*.** The startle eye blink reflex was measured according to Blumenthal et al.'s guidelines (2005). Two small Ag/AgCL electrodes (5 mm) were placed over the orbicularis oculi muscle of the left eye, while a ground electrode was placed in the middle of the forehead. The raw EMG signal

was amplified with a gain of 5000, filtered with a hardware band pass filter of 0.5 – 500 Hz, and digitally sampled at 1000 Hz, later offline rectified and integrated with PSPHA (De Clercq, Verschuere, De Vlieger, & Crombez, 2006). The magnitude of the eye blink amplitude was computed as the subtraction of the mean rectified baseline value (0 – 20 ms after probe onset) from the rectified peak value in the 21 – 120 ms interval after probe onset. Trials on which baseline values deviated more than 2.5 *SD* from the mean baseline value of the subject were visually inspected, and if necessary (e.g., movement artefacts, blink onset before probe onset), eliminated (11.74 %). Finally, reflex magnitudes were converted to *T*-scores across trials on a within-participant basis to adjust for between-participant differences in response and baseline EMG magnitude (Funayama, Grillon, Davis, & Phelps, 2001) as follows: *z*-score value = (raw magnitude value – *M* all raw values)/*SD* all raw values; *T*-score value = (*z*-score value x 10) + 50. *Z*-score values were trimmed (all scores below -3 and above +3 were put at -3 and +3 respectively) before they were converted to *T*-scores.

Additional measures of the autonomous nervous system (ANS). We measured two additional implicit measures, namely skin conductance and heart rate changes, both indices of autonomic functioning that have been shown to be responsive to negative emotional stimuli (Bradley, Codispoti, Cuthbert, & Lang, 2001).

Skin conductance was measured using a constant voltage (0.5 V) and two Ag/AgCL electrodes with a diameter of 8 mm. The electrodes were filled with conductive gel and were attached on the thenar and hypothenar eminences of the left hand. Skin conductance was digitized at 10 Hz for the entire duration of the pain movie (8000 ms). Using PSPHA, skin conductance responses were calculated as the difference between the highest and the lowest value in this 8000 ms time window. In order to normalise the data, skin conductance

amplitudes were square root transformed prior to analysis (Dawson, Schell, & Fillion, 2000).

Finally, heart rate was measured using three Ag/AgCL electrodes with a diameter of 8 mm filled with conductive gel and placed in lead II configuration (by attaching electrodes to both legs and the right arm, heart rate is measures as the voltage drop from left leg to right arm). The heart rate was filtered (band pass: 0 – 40 Hz) and digitized at 500 Hz. For heart rate changes, PSPHA was used to detect R-peaks, to calculate the distance between them (inter beta interval; IBI), and to correct for artefacts. Prior to analysis, the IBI was converted to heart rate in beats per minute (bpm) per real-time epoch (1000 ms). Mean bpm in the first 1000 ms of the video clip was compared to the mean bpm of the following 7000 ms, by calculating mean heart rate change (i.e. mean heart rate last 7000 ms – mean heart rate first 1000 ms).

Results

A .05 significance level was used in all statistical tests. Due to equipment failure, physiological recording was limited to 15 subjects for all physiological measures.

Subjective reports. All four questions followed the expected pattern, resulting in higher scores after imitation compared to non-imitation blocks (see Table 2). A 2 (Condition: Imitation versus Non-imitation) x 4 (Item: 1 - 4) repeated measures analysis, however, showed a significant Condition by Item interaction, $F(3,17) = 3.75$, $p < .05$. Planned comparisons indicated that conditions differed only for the affective-other and self-sensory questions, $t(19) = 2.21$, $p < .05$, $d = .40$ and $t(19) = 3.25$, $p < .01$, $d = .44$ respectively, but not for the other two questions (both ps > .05).

Table 2: Four behavioural questions, the aspect of empathy for pain they refer to, and their corresponding mean scores (standard deviations) in the different conditions (range from -5 to +5).

Question	Aspect	Imitation	Non-imitation
'How unpleasant do you think the other person found the pain stimulation?'	Other – affective	4.30 (.49)	4.18 (.61)
'How intense do you think the other person experienced painful sensations?'	Other – sensory	4.15 (.59)	4.07 (.65)
'How unpleasant did you find the pain stimulation yourself?'	Self – affective	2.02 (2.42)	1.86 (2.30)
'How intense did you experience painful sensations yourself?'	Self – sensory	.17 (2.87)	-.47 (2.85)

Blink modulation and ANS activity. A paired *t*-test revealed a significant difference in startle magnitude between the imitation and non-imitation condition: $t(14) = 3.41$, $p < .01$, $d = 3.35$; with higher scores after imitation compared to non-imitation blocks (see Figure 2).

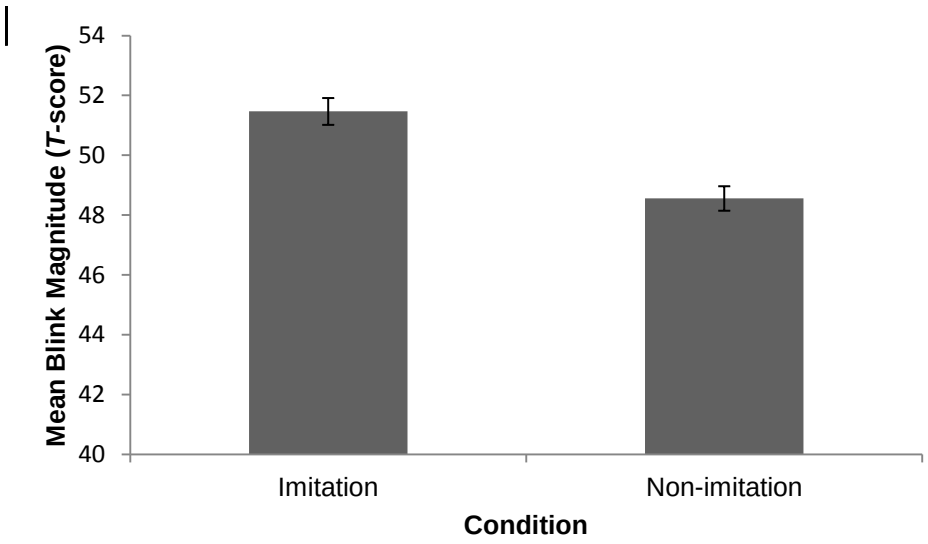


Figure 2: Mean blink magnitude in the imitation and non-imitation condition in the first experiment. Magnitude is expressed as within subjects *T*-scores, error bars are standard errors of the mean.

Interestingly, there were no significant correlations between behavioural and physiological data, nor were there any significant correlations with subjects' scores on the sub-scales of the IRI. Furthermore, IRI scale scores were added as covariates in all analyses to investigate the moderating effect of dispositional empathic tendencies. Interactions with these sub-scores were again not significant for both explicit and implicit responses (all *p*s > .05).

In contrast to the startle blink reflex, skin conductance and heart rate changes were not sensitive to the imitation manipulation (*p*s >.05). This was not completely surprising, however, given that the startle blink reflex amplitude has been shown to be most sensitive to changes in valence (Bradley, 2009).

Discussion

The aim of this first experiment was to investigate whether being imitated has an influence on the way we react to perceiving pain in others. Using behavioural and physiological measures, the present study provides evidence for the hypothesis that being imitated leads to higher affective responses when observing pain. On the behavioural level, participants judged that the other person experienced the pain stimulation as more unpleasant and that they experienced more intense painful sensations themselves after being imitated. Furthermore, the startle blink magnitude was significantly larger when viewing the pain movie after being imitated, indicating that higher negative affect was elicited in this condition. This indicates a stronger pain-related response after being imitated compared to not being imitated. Since Preston and de Waal (2002) argue that observing pain can lead to associated physiological responses as an index of higher activation in pain-related brain areas, and since the startle reflex has previously been related to empathy for pain (Caes et al., 2012), we believe that our results provide evidence for the idea that being imitated increases empathy for pain.

The question remains, however, which mechanism(s) could underlie the increase of empathy for pain when being imitated. First, social-psychological research suggests that being imitated leads to enhanced liking for the other person (Chartrand & Bargh, 1999). This increased liking could in turn lead to higher empathy for pain, since it has been shown that reactions to observing another person in pain are stronger when we have an affective relationship with the person observed (Cheng et al., 2010; Hein, Silani, Preuschoff, Batson, & Singer, 2010). A second mechanism, however, is strongly based on the idea of shared representations, and suggests that the underlying process combining imitation and observational pain research is more basic in nature. As suggested above, both motor imitation and empathy for pain rely on shared representations

of self and other, possibly eliciting a self-other confusion mechanism (e.g. Brass, Derrfuss, Cramon, & von Cramon, 2003; Liepelt, von Cramon, & Brass, 2008). In the imitative condition, this confusion is thought to be elicited, since the same actions are performed and these actions are commonly coded. Furthermore, when representations of self and other become difficult to distinguish, pain applied to the other person should have a stronger influence on your own bodily reactions. Note that the current setup (using no delay between executed and observed movement and a first person perspective) increased the likelihood that this self-other confusion mechanism would take place. However, since significant effects on the ratings were observed for items suggesting both an abstract empathy process (affective-other question) and self-other confusion (sensory-self question), it is difficult to distinguish between both accounts based on the present results. Furthermore, the absence of correlations between subjective reports and implicit responses suggests that multiple mechanisms may be at work, although our relatively small sample size might be responsible for the absence of correlations in this experiment as well. The finding that being imitated changed empathy for pain on a trial by trial basis, however, is more in accordance with a self-other confusion interpretation rather than a trial by trial change in liking.

Hence, to further investigate the possible influence of an underlying self-other confusion mechanism based on shared representations between self and other, we conducted a second experiment in which we aimed to explore this process in more depth, and gain better insight into the effects observed in the first experiment. The general logic of the second experiment was thus to link observed effects of the first experiment to processes related to confusion between self and other, and investigate whether the strength of empathy for pain would be affected by increasing this self-other overlap.

EXPERIMENT 2

In the second experiment, we aimed to replicate as well as extend the findings of the first study. To do so, we linked our setup to rubber hand illusion (RHI) paradigms, in which subjects feel ownership over a rubber hand when viewing this rubber hand being stroked simultaneously with their own hidden hand (Botvinick & Cohen, 1998). This illusion, commonly observed with a sensory manipulation, is also thought to reflect sharing of representations between self and other (e.g. Tajadura-Jiminez, Grehl, & Tsakiris, 2012). First, we wanted to investigate whether the setup we have used in Experiment 1 with the hand being presented on a computer screen positioned in front of participants elicits a stronger RHI in the imitative compared to the non-imitative condition (see Dummer, Picot-Annand, Neal, & Moore, 2009 for a similar action-induced RHI). Second, we also wanted to explore whether we could create a setup which would increase self-other confusion by manipulating the spatial position of the observed hand. Hence, we varied our original setup as explained in Experiment 1 by tilting the screen on which the videotaped right hand was presented and placing participants' own right hand under it, covering the latter and thus making it invisible (in contrast to the first setup where the screen was placed in front of participants). Since these adjustments were thought to elicit a stronger RHI (as do similar manipulations with a sensory RHI; Lloyd, 2007) and thus enhance confusion between self and other, we expected effects of being imitated on empathy for pain to be stronger in this newly developed setup compared to the original one. This way, we wanted to investigate whether self-other confusion might (in part) be responsible for the observed effects.

Method

Participants. Twenty-one right-handed volunteers (M_{age} = 21.38, *SD* = 2.36) participated in this second study, all with normal or corrected-to-normal vision. To control for possible sex differences, only female volunteers were recruited. They were given 10 Euros for participation, and provided written consent at the beginning of the experiment. The study was granted ethical approval by the local ethics committee.

Experimental design. The second experiment consisted of two parts in a within-subjects design. In one part, participants performed the task with a setup equal to that of the first experiment (setup where hand of participant lies in front of the screen: "front" position setup), while a slightly different setup was used in the other part of the experiment (setup where hand of participant lies under the screen: "under" position setup). The order of these parts was counterbalanced across participants: odd subjects started with the front position setup, while even subjects started with the under position setup. Furthermore, an additional movie was used in this study ('knife': knife cuts the hand). This way, ten movies were available, of which two times five different movies were randomly allocated to one of both setups for all participants. Since the experimental design was equal to that of the first experiment in both parts, each part consisted of 20 trials (five pain movies combined with two imitative and two startle conditions).

Stimuli and apparatus. The video material was equal to that of the first experiment, with the addition of a tenth pain movie (knife movie, see above).

Participants performed the task as explained in Experiment 1 under two setups with a different spatial position: hand in front of and under the screen. In the front position setup, the screen on which all stimuli material was presented was placed in front of participants. This way, participants' own hand was still visible. In the under position setup, on the other hand, the same screen was

tilted horizontally, and participants were asked to place their hand under the screen. To ensure that subjects could only see the hand on screen, a towel was attached to the screen, covering their own hand.

Self-report measures. In contrast to the first experiment, 11 explicit questions were presented after each pain movie, in order to get a better understanding of possible underlying self-other confusion and RHI processes. The first three questions, to be rated on a scale from -5 to +5 were used to examine whether a RHI was elicited, questioning three different aspects of this illusion (Longo, Schuur, Kammers, Tsakiris, & Haggard, 2008; Tsakiris, Longo, & Haggard, 2010): *'It felt as if I could control the hand on screen'* (agency)*, 'It felt as if my own hand was at the location of the hand on screen'* (location)*, 'It felt as if the hand on screen was my own hand'* (ownership). Furthermore, a fourth question, referring to empathy for pain, had to be answered: *'I felt pain on my own hand when I saw the hand on screen being injured'.* Finally, a Dutch translation of the scale of Batson, Fultz, and Schoenrade (1987) was used, presenting seven items measuring two types of emotional responses. These items questioned the subjective feelings of participants while viewing painful stimulation, with four items referring to self-oriented feelings (personal distress; *'While viewing the painful stimulation of the other person I felt worried/distressed/anxious/sad'*), and three items referring to other-oriented feelings (concern; *'While viewing the painful stimulation of the other person I felt understanding/empathetic/compassionate'*). As such, questions referring to the observed painful situations could be divided into two categories: self (specific question referring to pain + self-items of the Batson scale, Cronbach's $\alpha > .90$) versus other (other-items of the Batson scale, Cronbach's $\alpha > .90$).

After the experiment, participants again filled in the IRI (Cronbach's α Perspective Taking = .82, Empathic Concern = .42, Fantasy = .85, Personal Distress = .84).

Procedure. The procedure was equal to the procedure of Experiment 1, with the exception that subjects performed the task under both a front and under position setup. Furthermore, participants now performed a random number of movements between 15 and 20 to decrease the length of the experiment.

Results

A .05 significance level was used in all statistical tests. Behavioural outliers were defined as subjects deviating more than 2.5 *SD* on their general RHI score from the general mean of this score ($n = 1$; this subject was discarded from all further analyses). Due to equipment failure, physiological recording was limited to 19 subjects for all physiological measures.

Subjective Reports. First, the behavioural questions referring to aspects of the RHI were inspected to verify which dimensions of the illusion were successfully elicited. However, since all items were strongly correlated (all ps < .05) and all items showed the same pattern, a general RHI score was calculated as the mean of the scores on these three items taken together, allowing us to use this single score in all further analyses (Cronbach's $\alpha > .81$). A 2 (Position: Front versus Under) x 2 (Condition: Imitation versus Non-imitation) repeated measures analysis showed a significant main effect of Position, $F(1,19) = 4.25$, $p < .05$, $d = .60$ General RHI scores were higher in the under position setup than in the front position setup. Furthermore, the main effect of Condition, $F(1,19) = 68.27$, $p < .001$, $d = 4.25$ was also significant; while its interaction with Position was not, $F(1,19) < 1$. Scores were significantly higher in the imitative condition than in the non-imitative condition for both positions (see Figure 3).

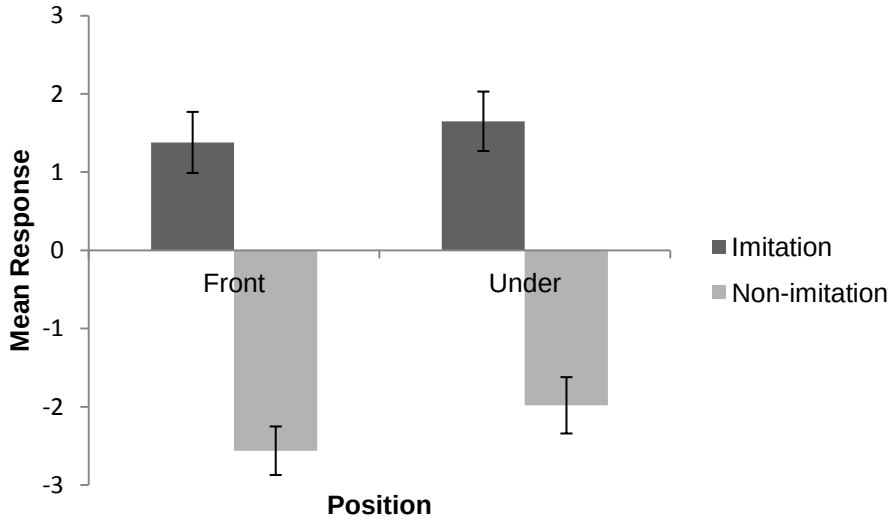


Figure 3: Mean general RHI scores (range from -5 to +5) in the imitation and non-imitation condition in the front and under position setup in the second experiment. Error bars are standard errors of the mean.

Second, all items questioning empathy for pain were divided into self- and other-related questions (see above), and analyzed by means of a 2 (Position: Front versus Under) x 2 (Condition: Imitation versus Non-imitation) x 2 (Perspective: Self versus Other) repeated measures analysis. Only a main effect of Condition, $F(1,19) = 15.57$, $p = .001$, $d = .60$ and Perspective, $F(1,19) = 12.00$, $p < .01$, $d = 1.00$, were observed (all other ps $> .05$). Higher scores were found in the imitative compared to the non-imitative condition (see Figure 4), and for other- compared to self-related items.

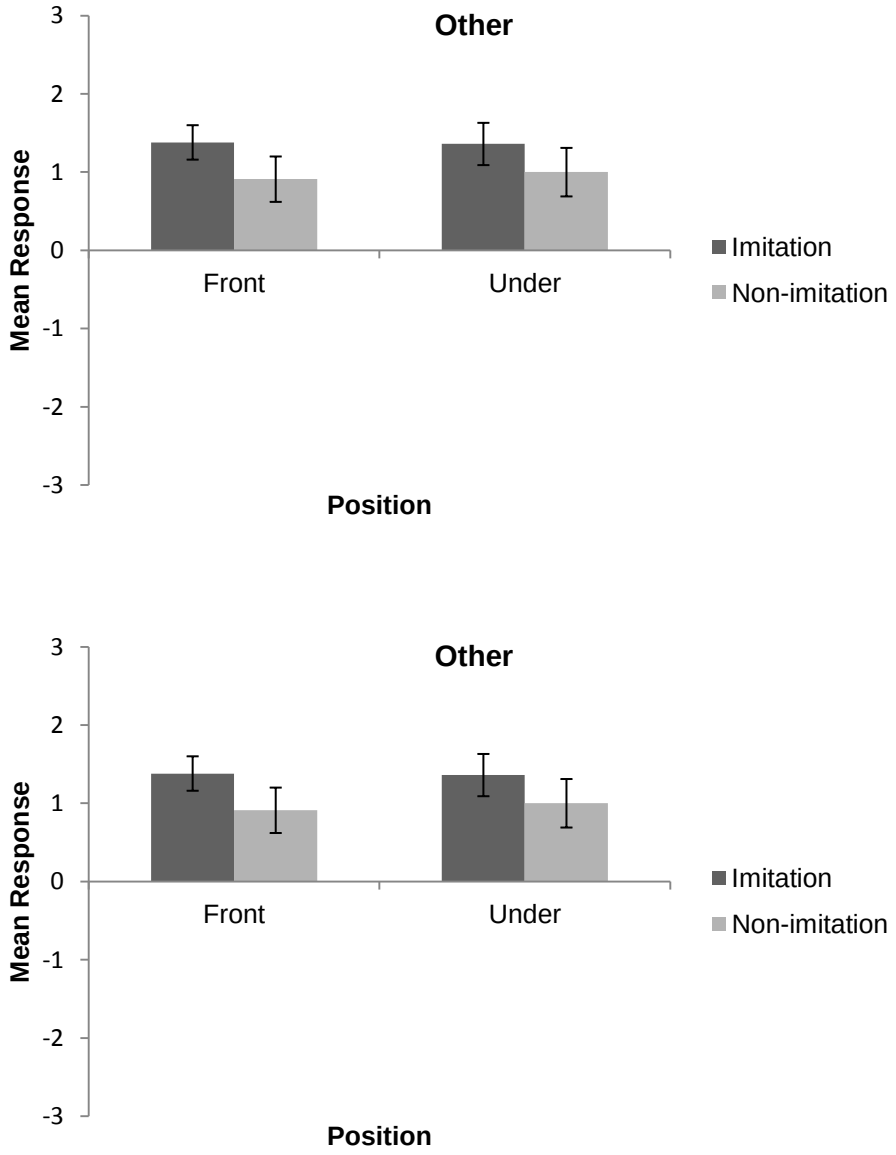


Figure 4: Mean scores (range from -5 to +5) in the imitation and non-imitation condition in the front and under position setup in the second experiment, for other- and self-related items referring to pain. Error bars are standard errors of the mean.

However, in order to test whether the imitation effect could be explained by self-other confusion, we performed a secondary mediation analysis investigating whether the effect of Condition on our dependent variables (other- and self-related behavioural scores) could be explained by RHI measures. For each participant, a RHI effect was calculated as the difference between general RHI scores in the imitation condition and the non-imitation condition, irrespective of positional setup (RHI effect = general RHI score in the imitation condition – general RHI score in the non-imitation condition). For this mediation analysis, we used a bootstrapping method following the procedure described by Preacher and Hayes (Hayes, 2009; Preacher & Hayes, 2004), a non-parametric resampling procedure. Figure 5 represents the effects and their corresponding weights that must be distinguished to perform the mediation analysis (only the outcome 'other-related items' is mentioned in the figure, however, the figure is applicable for all outcomes). The direct effect of Condition on other-related scores has the weight c', whereas the indirect effect, through the proposed mediator 'RHI effect' has the weight ab. The effect of Condition on RHI effect is represented by weight a, while weight b is the effect of RHI effect on other-related items, partialling out the effect of Condition. The total effect c of Condition on other-related items consists of both the direct (c') and the indirect (ab) effect. In the bootstrap analyses, the indirect effect ab is found to be significant if the bootstrap confidence interval excludes zero. Overall, mediation is assumed if 1) the total effect c is significant in addition to the indirect effect ab, and 2) the total effect c reduces significantly when controlling for the indirect effect ab (i.e. c' is non-significant).

Bootstrap analyses (with 5000 resamples) for RHI effect as a mediator in the relation between Condition and other- and self-related items resulted in a significant total effect of Condition upon these items ($c = .39$, $SE = .27$, $p < .05$ and $c = .47$, $SE = .35$, $p < .05$ respectively), but no direct effect of Condition (c'

= .51, SE = .34, p > .05 and c' = .66, SE = .45, p > .05). Furthermore, a direct effect of Condition upon RHI effect was found (a = 3.65, SE = .39, p < .001 and a = 3.65, SE = .39, p < .001 for other- and self-related items), indicating that a higher RHI effect was found in the imitation compared to the non-imitation condition. A direct effect of RHI effect on other- and self-related items was also found (b = .25, SE = .06, p < .001 and b = .31, SE = .08, p < .001), showing that a higher RHI effect resulted in higher self-report scores. Furthermore, the indirect effect of Condition on the dependent variable through the RHI effect was significant (ab = .90, SE = .23 and ab = 1.12, SE = .31) as the bootstrapped confidence interval excluded zero (90 % CI = .58 to 1.35 and 90 % CI = .65 to 1.70 respectively). Finally, there were significant positive correlations between the RHI effect and effects on the other- and self-related scores: r = .44, p < .05 and r = .38, p < .05 respectively.

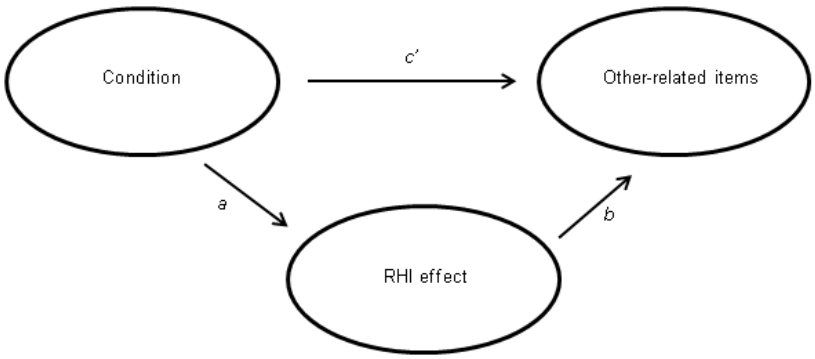


Figure 5: Effects and their corresponding weights in the mediation model. The total effect (*c*) consists of both the direct effect (*c'*) and the indirect effect (*ab*). The figure is applicable to all outcomes.

Blink modulation and ANS activity. A 2 (Position: Front versus Under) x 2 (Condition: Imitation versus Non-imitation) repeated measures analysis of the eye blink data revealed a significant main effect of Condition, $F(1,18) = 11.53$, $p < .01$, $d = 2.72$. The main effect of Position and its interaction with Condition, however, were non-significant (both Fs < 1; see Figure 6). Performing the same mediation analysis as mentioned above for self-report measures with blink data as dependent variable resulted in similar results. Bootstrap analyses resulted in a significant total effect of Condition upon eye blink data (c = 3.78, SE = .79, p < .001), but no direct effect of Condition (c' = 2.68, SE = 1.10, p > .05). Furthermore, a direct effect of Condition upon RHI effect was found (a = 3.60, SE = .43, p < .001), while a direct effect of RHI effect on eye blink data was also found (b = .31, SE = .22, p < .05). Finally, the indirect effect of Condition on the dependent variable through the RHI effect was significant (ab = 1.10, SE = .87) as the bootstrapped confidence interval excluded zero (90 % CI = .28 to 2.61).Performing the same analysis with the other behavioural effects (effects of other- and self-related items) as mediators did not lead to a mediation pattern.

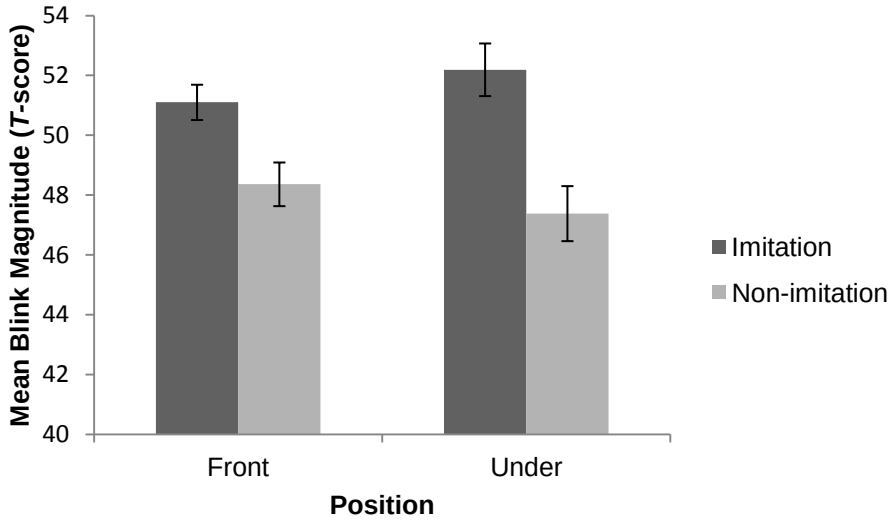


Figure 6: Mean blink magnitude in the imitation and non-imitation condition in the front and under position setup in the second experiment. Magnitude is expressed as within subjects *T*-scores, error bars are standard errors of the mean.

Heart rate data was again insensitive to our manipulation (*p*s > .05), but skin conductance data did show similar effects as startle blink data in this experiment. The same 2 (Position: Front versus Under) x 2 (Condition: Imitation versus Non-imitation) repeated measures analysis only showed a significant main effect of Condition, $F(1,18) = 4.56$, $p < .05$, $d = .61$ (see Figure 7). However, a mediation analysis with the behavioural RHI effect (but not with the other behavioural effects) revealed a significant total effect of Condition upon skin conductance responses (c = .19, SE = .12, p < .001), but no direct effect of Condition (c' = .42, SE = .15, p > .05). Furthermore, a direct effect of Condition upon RHI effect was found (a = 3.34, SE = .41, p < .001). A direct effect of RHI effect on skin conductance data was also found (b = .07, SE = .03, p < .05). Finally, the indirect effect of Condition on the dependent variable

through the RHI effect was significant (ab = .23, SE = .11) as the bootstrapped confidence interval excluded zero (90 % CI = .06 to .44).

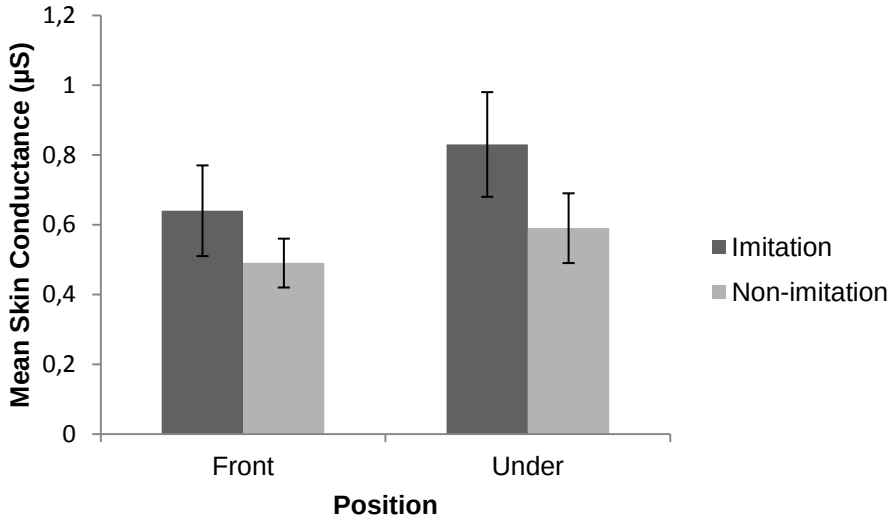


Figure 7: Mean skin conductance in the imitation and non-imitation condition in the front and under position setup in the second experiment. Skin conductance responses are expressed as the difference between the highest and the lowest value in a specified time window, and error bars are standard errors of the mean.

Interestingly, there were again no significant correlations between behavioural and physiological data, nor were there any correlations or interactions with subjects' scores on the sub-scales of the IRI (all *p*s > .05). Furthermore, no correlations between these IRI scales and the behavioural RHI effect were observed (all *p*s > .05).

Discussion

In this second experiment, we replicated as well as extended findings of the first experiment. First, behavioural and physiological measures in two

setups both confirmed the hypothesis that being imitated enhances affective responses when seeing someone else in pain. On the behavioural side, ratings on other- and self-related items after viewing the pain movies were higher when participants were being imitated during the action phase. Furthermore, mean blink magnitude and mean skin conductance responses were also higher in the imitation condition, indicating higher physiological affective responding when viewing someone else in pain after being imitated. However, we did not find a difference between the two setups we used in this experiment: both the setup where hands of participants were placed in front of the screen and the setup where participants' hands were placed under this screen showed stronger responses in the imitation condition, without interaction between the two setups. This was somewhat unexpected, since research using sensory RHI paradigms has shown that a more congruent spatial position between own and rubber hand elicits the strongest RHI (Lloyd, 2007), and we expected this to result in higher empathy for pain due to increased self-other confusion. In this experiment, behavioural results indicated that both the front and under position setup elicited a very strong RHI in the imitation condition, and that this illusion was indeed slightly stronger in the setup with the most congruent spatial position. Although this suggests that our spatial position manipulation was successful, it seems that this stronger RHI in the under position setup failed to elicit stronger affective responding when viewing someone else in pain.

A more in depth analysis of the results, however, revealed that the imitation effect on affective responding when viewing someone else in pain disappeared when taking the behavioural RHI effect into account. Since similar analyses with the other behavioural effects did not result in this disappearance, this suggests that the differences in affective responses between the imitative and the non-imitative condition could – at least in part – be accounted for by the RHI that was very strongly elicited when being imitated. It thus seems that the

RHI (or self-other confusion) elicited in the imitation condition might have been responsible for the effect of imitation on empathy for pain, but that this effect could not be enhanced by a spatial position manipulation that increased the illusion. We believe that this was due to the fact that the imitation condition elicited a very strong RHI in both the front and under position setup, indicating that this effect was still robust under a spatial incongruent position, and might have already reached its limit in this condition. In a recent paper, Kalckert and Ehrsson (2012) used a similar motor-induced RHI and measured both agency and ownership over the rubber hand. When varying the spatial position with a 180 degree rotation, ownership over this rubber hand diminished while agency remained very strong. Our results were not able to distinguish between ownership and agency, since both aspects of the RHI seemed to be elicited in the imitation condition in both spatial positions. However, since the hand in the front position setup was not completely incongruent with the position of the own hand, our spatial manipulation was not as strong as the one used by Kalckert and Ehrrson (2012). Nevertheless, both our study and the research of Kalckert and Ehrrson (2012) suggest that (some) measures of the RHI are invariant to spatial manipulations.

GENERAL DISCUSSION

In this study, we have shown in two different experiments that being imitated leads to higher affective responding when seeing someone else in pain, both on an explicit behavioural and an implicit physiological level. Behavioural scores of empathy for pain were higher when subjects were being imitated in both experiments. Furthermore, we replicated the finding that startle blink

magnitude when viewing a painful movie is higher after being imitated, indicating stronger negative affect in this condition. Finally, the second experiment suggested that skin conductance (as an index of ANS activity) was also higher in an imitative situation, again providing evidence for stronger affective responding when viewing someone in pain after being imitated.

In the second experiment, we related our setup to RHI paradigms in order to investigate a self-other confusion mechanism. We measured the RHI in our paradigm, and induced a position manipulation which was thought to increase this illusion. Furthermore, we expected a stronger RHI to be related to stronger empathy for pain. In this experiment we found an influence of both the position of the setup and imitative condition on the RHI, but not the predicted interaction between position and condition which we expected from a self-other confusion account. Furthermore, we found a strong effect of imitative condition on our measures of empathy for pain, whereas we did not find an interaction between condition and position of the setup. However, although we did not find evidence for this interaction, secondary analyses in which it was shown that imitation effects are mediated by RHI measures, suggested that the sharing of representations between self and other might nevertheless be responsible for the observed results. These results indicated that being imitated elicited a very strong RHI, and that this effect accounted for the higher affective responding in this imitative situation. Although it has already been shown that a RHI can increase affective reactions when seeing a rubber hand in pain (Armel & Ramachandran, 2003; Ehrsson, 2007; Famer, Tajadure-Jiménez, & Tsakiris, 2012), it has never been shown with an action induced illusion like the one used in the current study. Furthermore, it was shown that our action-induced RHI was strongly influenced by the imitation manipulation in our paradigm, while the spatial manipulation was less important and did not seem to influence affective responding to painful stimuli. It seems that being imitated elicited a

strong RHI that influenced empathy for pain, and that this manipulation worked with both a spatially congruent and incongruent position.

It remains an important open question, however, whether a self-other confusion mechanism might be important in more complex social situations as well, where the link with the RHI might not be as evident as it was in our imitative setup. Furthermore, whereas social-psychological research has indicated that complex prosocial effects of being imitated only take place when subjects are unaware of the imitative situation (Chartrand & Bargh, 1999; van Baaren, Holland, Kawakami, & van Knippenberg, 2004), the imitation versus non-imitation situation was completely transparent in the current study. Due to the absence of a delay between executed and observed movement, the basic simplicity of these movements, and the usage of a first person perspective, it was immediately clear to participants whether they were being imitated or not. However, a study by Singer et al. (2008) indicates that prosocial behaviour and empathy are not necessarily positively correlated. As such, while lack of awareness of imitation seems necessary to elicit prosocial behaviour, our study indicates that empathy for pain is more immune to such a top-down modulation, and can be influenced by transparent imitative situations. This might suggest that the shared representational system acts differently under different social situations, and it remains to be investigated why and how this is the case. One possibility is that in social-psychological research, awareness of being imitated induces reactance because people get the impression of being mocked by the imitator. This is obviously not true in the present setup. Thus, it seems that the influence of being imitated on basic processes such as empathy for pain remains strong despite awareness in a setup where self-other confusion is thought to underlie the effects. It has to be noted, however, that we might not be able to generalize the results found in our particular setup to more ecologically valid situations. As mentioned above, several choices were made in order to increase

self-other confusion that might have resulted in an important discrepancy between our setup and complex imitative situations. Furthermore, whereas social-psychological research usually employs real-life social interactions, the effects observed in the present study where based on the interaction with a previously videotaped hand on screen (both in the action and pain perception phase), without providing any social context. Importantly, pain perception research has indicated that online social interactions and movie- or picture-based interactions activate both converging and diverging brain areas, with a core network including the anterior cingulated cortex (ACC) and bilateral anterior insula (AI) activated most consistently over all situations (Lamm, Decety, & Singer, 2011; Zaki & Ochsner, 2012). Furthermore, Perani et al. (2001) have also shown that virtual social interactions (e.g. using video clips) are associated with only part of the action observation network activated in natural social interactions. However, research on automatic imitation has consistently shown that these effects are very strong with videotaped hands (e.g. Brass et al., 2000; Brass et al., 2001). Furthermore, it has been demonstrated that participants attribute intentionality to these videotaped hands since manipulating this belief leads to a reduction of automatic imitation effects (Liepelt et al., 2008). Research by Hogeveen and Obhi (2012) has additionally shown that naturalistic social interaction and action observation of human actions involve common motor resonance mechanisms. Finally, Kalckert and Ehrsson (2012) have shown that only the feeling of ownership, but not of agency, is preserved when changing a rubber hand from a first to a third person perspective, suggesting that the mechanisms in both perspectives are at least partially different. Since we used a first person perspective setup, this would suggest that our paradigm might not be entirely suitable to explain common third person imitative experiences. Thus, it is clear that our operationalization of being imitated shows discrepancies with those used in social-psychological

research on related phenomena in naturalistic environments. Furthermore, the temporal contingency that is present in both experimental conditions in our setup (being imitated and not being imitated) also forces us to think about future research exploring what happens when a control condition is included in which no contingent reaction of the hand on screen is present (e.g. seeing a hand that never moves, or without any systematic relationship to the subjects' movements) in order to distinguish positive effects of being imitated compared to negative effects of not being imitated. Although we recognize all these setup-related differences to classical social-psychological paradigms, we nevertheless believe that our study might be important in understanding social (imitative) interactions, especially since all studies mentioned above show – next to diverging activations – partially overlapping areas being activated when comparing real-life and experimentally induced interactions as well. However, we also believe it is important to further investigate all these aspects in more depth, and explore in which social interactions a mechanism assuming overlapping self-other representations might be relevant.

Another important limitation of the study is the indirect nature in which empathy for pain is measured. Therefore, future research is needed to investigate directly whether being imitated leads to stronger activation of pain-related brain areas with brain imaging techniques. Research indicates that the affective-motivational dimensions of pain, including the bilateral AI and the dorsal ACC, are most consistently activated when seeing someone else in pain (Singer et al., 2004; Lamm et al., 2011). However, some studies suggest that the sensory dimensions of pain are affected in these situations as well (Keysers et al., 2010; Loggia et al., 2008). Based on the present results, we would expect affective (and sensory) parts of the pain matrix to show stronger activation when seeing someone else in pain after being imitated compared to not being imitated. Furthermore, regions such as the temporal parietal junction and the

medial prefrontal cortex have been related to shared representational processes such as self-other distinction (Decety, Chaminade, Grèzes, & Meltzoff, 2002; Farrer & Frith, 2002; Spengler, von Cramon, & Brass, 2010). Since there is an obvious link between these mechanisms and the account used to explain the results in the present paper, we think it warranted to explore the involvement of these regions in our paradigm as well.

As a final comment, we would like to point out that it is somewhat disputable whether the term 'empathy for pain' is adequate to describe the results in our study, since empathy requires the ability to experience feelings of the other person while at the same time being able to recognize this person as another entity. A self-other confusion process, which we believe to be the underlying mechanism of the effects in our study, would suggest otherwise. However, although our autonomic results suggest that there is self-other confusion at an implicit level, our behavioural results in both experiments indicate that people still consciously seem to distinguish self from other. Responses to other- and self-related questions were differently rated, with higher scores on other-related than on self-related subjective judgments. This suggests that self-other confusion was not complete, and we therefore opted to use the term empathy for pain nevertheless. However, our results suggest that this term might not encompass the whole process.

To summarize, our data suggest that being imitated leads to a stronger affective response when seeing someone else in pain. This suggests a tight link between shared representation on the motor and the sensory level.

REFERENCES

Armel, K. C., & Ramachandran, V. S. (2003). Projecting sensations to external objects: evidence from skin conductance response. *Proceedings of the Royal Society of London B – Biological Sciences, 270,* 1499-1506. doi: 10.1098/rspb.2003.2364

Bastiaansen, J. A. C. J. Thioux, M., & Keysers, C. (2009). Evidence for mirror systems in emotions. *Philosophical Transactions of the Royal Society B – Biological Sciences, 364,* 2391-2404. doi: 10.1098/rstb.2009.0058

Batson, C. D., Fultz, J., & Schoenrade, P. A. (1987). Distress and empathy – 2 qualitatively distinct vicarious emotions with different motivational consequences. *Journal of Personality, 55,* 19-39. doi: 10.1111/ 1467-6494.ep8970569

Blumenthal, T. D., Cuthbert, B. N., Filion, D. L., Hackley, S., Lipp, O. V., & Van Boxtel, A. (2005). Committee report: Guidelines for human startle eyeblink electromyographic studies. *Psychophysiology, 42,* 1-15. doi: 10.1111/ j.1469-8986.2005.00271.x

Botvinick, M., & Cohen, J. (1998). Rubber hands 'feel' touch that eyes see. *Nature, 391,* 756- 756. doi:10.1038/35784

Bradley, M. M. (2009). Natural selective attention: Orienting and emotion. *Psychophysiology, 46,* 1-11. doi: 10.1111/j.1469-8986.2008.00702.x

Bradley, M. M., Codispoti, M., Cuthbert, B. N., & Lang, P. J. (2001). Emotion and motivation I: Defensive and appetitive reactions in picture processing. *Emotion, 1,* 276-298. doi: 10.1037/1528-3542.1.3.276

Brass, M., Bekkering, H., & Prinz, W. (2001). Movement observation affects movement execution in a simple response task. *Acta Psychologica, 106,* 3-22. doi: 10.1016/S0001-6918(00)00024-X

Brass, M., Bekkering, H., Wohlschläger, A., & Prinz, W. (2000). Compatibility between Observed and Executed Finger Movements: Comparing Symbolic, Spatial, and Imitative Cues. *Brain and Cognition, 44,* 124-143. doi: 10.1006/brcg.2000.1225

Brass, M., Derrfuss, J., Cramon, G. M. V., & von Cramon, D. Y. (2003). Imitative response tendencies in patients with frontal brain lesions. *Neuropsychology, 17,* 265-271. doi: 10.1037/0894-4105.17.2.265

Brass, M., & Heyes, C. M. (2005). Imitation: Is cognitive neuroscience solving the correspondence problem? *Trends in Cognitive Science, 9,* 489-495. doi: 10.1016/j.tics.2005.08.007

Bufalari, I., Aprile, T., Avenanti, A., Di Russo, F., & Aglioti, S. M. (2007). Empathy for pain and touch in the human somatosensory cortex. *Cerebral Cortex, 17,* 2553-2561. doi: 10.1093/cercor/bh1161

Caes, L., Uzieblo, K., Crombez, G., De Ruddere, L., Vervoort, T., & Goubert, L. (2012). Negative emotional responses elicited by the anticipation of pain in others: psychophysiological evidence. *The Journal of Pain, 13,* 467-476. doi: 10.1016/j.jpain.2012.02.003

Chartrand, T. L., & Bargh, J. A. (1999). The Chameleon effect: The perception-behaviour link and social interaction. *Journal of Personality and Social Psychology, 76,* 893-910. doi: 10.1037/0022-3514.76.6.893

Chartrand, T. L., & van Baaren, R. (2009). Human mimcry. *Advances in experimental social psychology, 41,* 219-274. doi: 10.1016/S0065-2601(08)00405-X

Cheng, Y. W., Chen, C. Y., Lin, C. P., Chou, K. H., & Decety, J. (2010). Love hurts: An fMRI study. *Neuroimage, 51,* 923-929. doi: 10.1016/j.neuroimage.2010.02.047

Cheng, Y., Lin, C-P., Liu, H-L., Hsu, Y-Y., Lim, K-E., Hung, D., & Decety, J. (2007). Expertise modulates the perception of pain in others. *Current Biology, 17,* 1708-1713. doi: 10.1016/j.cub.2007/09/020

Cheng, Y., Yang, C-Y., Lin, C-P., Lee, P-L., & Decety, J. (2008). The perception of pain in others suppresses somatosensory oscillations: A magnetoencephalography study. *Neuroimage, 40,* 1833-1840. doi: 10.1016/j.neuroimage.2008.01.064

Davis, M. H. (1980). A multidimensional approach to individual differences in empathy. *JSAS Catalog of Selected Documents in Psychology, 10,* 85.

Dawson, M. E., Schell, A. M., & Fillion, D. L. (2000). The electrodermal system. In J. T. Cacioppo, L. G. Tassinary & G. G. Berntson (Eds.), Handbook of psychophysiology (pp. 200-224). Cambridge: Cambridge University Press.

Decety, J., Chaminade, T., Grèzes, J., & Meltzoff, A. N. (2002). A PET exploration of the neural mechanisms involved in reciprocal imitation. *Neuroimage, 15,* 265-572. doi: 10.1006/nimg.2001.0938

Decety, J., Echols, S. C., & Correll, J. (2009). The blame game: the effect of responsibility and social stigma on empathy for pain. *Journal of Cognitive Neuroscience, 22,* 985-997. doi: 10.1162/jocn.2009.21266

Decety, J., & Lamm, C. (2006). Human empathy through the lens of social neuroscience. *The Scientific World Journal, 6,* 1146-1163. doi: 10.1100/tsw.2006.221

De Clercq, A., Verschuere, B., De Vlieger, P., & Crombez, G. (2006). Psychophysiological Analysis (PSPHA): A modular script-based program for analyzing psychophysiological data. *Behavior Research Methods, 38,* 504-510. doi: 10.3758/BF03192805

De Corte, K., Buysse, A., Verhofstadt, L. L., Roeyers, H., Ponnet, K., & Davis, M. H. (2007). Measuring empathic tendencies: reliability and validity of the Dutch version of the Interpersonal Reactivity Index. *Psychologica Belgica, 47,* 235-260.

de Vignemont, F., & Singer, T. (2006). The emapthic brain: How, when, and why? *Trends in Cognitive Sciences, 10,* 435-441. doi: 10.1016/j.tics.2006.08.008

Dummer, T., Picot-Annand, A., Neal, T., & Moore, C. (2009). Movement and the rubber hand illusion. *Perception, 38,* 271-280. doi: 10.1068/p5921

Ehrsson, H. H. (2007). The experimental induction of out-of-body experiences. *Science, 317,* 1048. doi: 10.1126/science.1142175

Farmer, H., Tajadura-Jiménez, A., & Tsakiris, M. (2012). Beyond the colour of my skin: How skin colour affects the sense of body-ownership. *Consciousness and Cognition, 21,* 1242-1256. doi: 10.1016/j.concog.2012.04.011

Farrer, C., & Frith, C. D. (2002). Experiencing oneself vs another person as being the cause of an action: the neural correlates of the experience of agency. *Neuroimage, 15,* 596-603. doi: 10.1006/nimg.2001.1009

Funayama, E. S., Grillon, C., Davis, M., & Phelps, E. A. (2001). A double dissociation in the affective modulation of startle in humans: Effects of unilateral temporal lobectomy. *Journal of Cognitive Neuroscience, 13,* 721-729. doi: 10.1162/08989290152541395

Goubert, L., Vervoort, T., & Craig, K. D. (in press). Empathy and pain. In R. F. Schmidt & G. F. Gebhart (Eds.), *Encyclopedia of Pain, Second Edition.* Heidelberg: Springer-Verlag.

Grezes, J., & Decety, J. (2001). Functional anatomy of execution, mental simulation, observation, and verb generation of actions: A meta-analysis. *Human Brain Mapping, 12,* 1-19. doi: 10.1002/1097-0193(200101)

Han, S. H., Fan, Y., & Mao, L. (2008). Gender difference in empathy for pain: an electrophysiological investigation. *Brain Research, 1196,* 85-93. doi: 10.1016/jbrainres.2007.12.062

Hawk, L. W., & Cook, E. W. (2000). Independence of valence modulation and prepulse inhibition of startle. *Psychophysiology,37,* 5-12. doi: 10.1111/1469-8986.3710005

Hayes, F. (2009). Beyond Baron and Kenny: statistical mediation analysis in the new millennium. *Communication Monographs, 76*, 408-420. doi: 10.1080/03637750903310360

Heberlein, A. S., & Atkinson, A. P. (2009). Neuroscientific evidence for simulation and shared substrates in emotion recognition. *Emotion Review, 1*, 162-177. doi:10.1177/1754073908100441

Hein, G., Silani, G., Preuschoff, K., Batson, C. D., & Singer, T. (2010). Neural responses to ingroup and outgroup members' suffering predict individual differences in costly helping. *Neuron, 68*, 149-160. doi: 10.1016/j.neuron.2010.09.003

Hein, G., & Singer, T. (2008). I feel how you feel but not always: The empathic brain and its modulation. *Current Opinion in Neurobiology, 18*, 153-158. doi: 10.1016/j.conb.2008.07.012

Hogeveen, J., & Obhi, S. S. (2012). Social interaction enhances motor resonance for observed human actions. *Journal of Neuroscience, 32*, 5984-5989. doi: 1523/JNEUROSCI.5938-11.2012

Jackson, P. L., Meltzoff, A. N., & Decety, J. (2005). How do we perceive the pain of others? A window into the neural processes involved in empathy. *Neuroimage, 24*, 771-779. doi: 10.1016/j.neuroimage.2004.09.006

Kalckert, A., & Ehrrson, H. H. (2012). Moving a rubber hand feels like your own: a dissocation of ownership and agency. *Frontiers in Human Neuroscience, 6*. doi: 10.3389/fnhum.2012.00040

Keysers, C., Kaas, J. H., & Gazzola, V. (2010). Somatosensation in social perception. *Nature Reviews Neuroscience, 11*, 417-428. doi: 10.1038/nrn2833

Kühn, S., Muller, B. C., van Baaren, R. B., Wietzker, A., Dijksterhuis, A., & Brass, M. (2010). Why do I like you when you behave like me? Neural mechanisms mediating positive consequences of observing someone being imitated. *Social Neuroscience, 5*, 384-392. doi: 10.1080/17470911003633750

Lakin, J. L., & Chartrand, T. L. (2003). Using nonconscious behavioral mimicry to create affiliation and rapport. *Psychological Science, 14*, 334-339. doi: 10.1111/1467-9280.14481

Lakin, J. L., Chartrand, T. L., & Arkin, R. M. (2008). I am too just like you – Nonconscious mimicry as an automatic behavioral response to social exclusion. *Psychological Science, 19*, 816-822. doi: 10.1111/j.1467-9280.2008.02162.x

Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage, 54*, 2492-2502. doi: 10.1016/j.neuroimage.2010.10.014

Lamm, C., Meltzoff, A. N., & Decety, J. (2010). How do we empathize with someone who is not like us? A functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience, 22*, 362-376. doi: 10.1162/jocn.2009.21186

Lamm, C., Nusbaum, H. C., Meltzoff, A. N., & Decety, J. (2007). What are you feeling? Using functional magnetic resonance imaging to assess the modulation of sensory and affective responses during empathy for pain. *PloS One, 12*: e 1292. doi: 10.1371/journal.pone.0001292

Liepelt, R., von Cramon, D. Y., & Brass, M. (2008). What Is Matched in Direct Matching? Intention Attribution Modulates Motor Priming. *Journal of Experimental Psychology: Human Perception and Performance, 34*, 578-591. doi: 10.1037/0096-1523.34.3.578

Lloyd, D. M. (2007). Spatial limits on referred touch to an alien limb may reflect boundaries of visuo-tactile peripersonal space surrounding the hand. *Brain and Cognition, 64,* 104-109. doi: 10.1016/j.bandc.2006.09.013

Loggia, M. L., Mogil, J. S., & Bushnell, M. C. (2008). Empathy hurts: Compassion for another increases both sensory and affective components of pain perception. *Pain, 136*, 168-176. doi: 10.1016/j.pain.2007.07.017

Longo, M. R., Schuur, F., Kammers, M. P. M., Tsakiris, M., & Haggard, P. (2008). What is embodiment? A psychometrix approach. *Cognition, 107*, 978-998. doi: 10.1016/j.cognition.2007.12.004

Miller, M. W., Patrick, C. J., & Levenston, G. K. (2002). Affective imagery and the startle response: Probing mechanisms of modulation during pleasant scenes, personal experiences, and discrete negative emotions. *Psychophysiology, 39*, 519-529. doi: 10.1017/S0048577202394095

Perani, D., Fazio, F., Borghese, N. A., Tettamanti, M., Ferrari, S., Decety, J., & Gilardi, M. C. (2001). Different brain correlates for watching real and virtual hand actions. *Neuroimage, 14*, 749-758. doi: 10.1006/nimg.2001.0872

Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behaviour Research Methods, 36*, 717-731. doi: 10.3758/BF03206553

Preston, S. D., & de Waal, F. B. M. (2002). Empathy: Its ultimate and proximate bases. *Behavioral Brain Science, 25*, 1-72. doi: 10.1017/S0140525X02000018

Singer, T., & Lamm, C . (2009). The Social Neuroscience of Empathy. *Annals of the New York Academy of Sciences, 1156*, 81-96. doi: 10.1111/j.1749-6632.2009.04418.x

Singer, T., Seymour, B., O' Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for Pain Involves the Affective but not Sensory Components of Pain. *Science, 303,* 1157-1162. doi: 10.1126/science.1093535

Singer, T., Seymour, B., O' Doherty, J. P., Stephan, K. E., Dolan, R. J., & Frith, C. D. (2006). Empathic neural responses are modulated by the perceived fairness of others. *Nature, 439,* 466-469. doi: 10.1038/nature04271

Singer, T., Snozzi, R., Bird, G., Petrovic, P., Silani, G., Heinrichs, M., & Dolan, R. J. (2008). Effects of oxytocin and prosocial behaviour on brain responses to direct and vicariously experienced pain. *Emotion, 8,* 781-791. doi: 10.1037/a0014195

Spengler, S., von Cramon, D. Y., & Brass, M. (2010). Resisting motor mimicry: Control of imitation involves processes central to social cognition in patients with frontal and temporo-parietal lesions. *Social Neuroscience, 5,* 401-416. doi: 10.1080/17470911003687905

Stel, M., van Baaren, R. B., & Vonk, R. (2008). Effects of mimicking: Acting prosocially by being emotionally moved. *European Journal of Social Psychology, 38,* 965-976. doi: 10.1002/ejsp.472

Tajadura-Jimenez, A., Grehl, S., & Tsakiris, M. (2012). The other in me: Interpersonal multisensory stimulation changes the mental representation of the self. *PLOS one, 7.* doi: 10.1371/journal.pone.0040682

Tsakiris, M., Longo, M.R., & Haggard, P. (2010). Having a body versus moving your body: Neural signatures of body-ownership. *Neuropsychologia, 48,* 2740-2749. doi: 10.1016/j.neuropsychologia.2010.05.021

van Baaren, R. B., Holland, R. W., Kawakami, K., & van Knippenberg, A. (2004). Mimicry and Prosocial Behavior. *Psychological Science, 15,* 71-74. doi: 10.1111/j.0963-7214.2004.01501012.x

Vrana, S. R., Spence, E. L., & Lang, P. J. (1988). The startle probe response: A new measure of emotion? *Journal of Abnormal Psychology, 97,* 487-491. doi: 10.1037/0021-843X.97.4.487

Xu, X. J., Zuo, X. Y., Wang, X. Y., & Han, S. H. (2009). Do you feel my pain? Racial group membership modulates empathic neural responses. *Journal of Neuroscience, 29,* 8525-8529. doi: 10.1523/JNEUROSC.2418-09.2009

Yang, C. Y., Decety, J., Lee, S. Y., Chen, C. Y., & Cheng, Y. W. (2009). Gender differences in the mu rhythm during empathy for pain: An electroencephalographic study. *Brain Research, 1252,* 176-184. doi: 10.1016/j.brainres.2008.11.062

Zaki, J., & Ochsner, K. (2012). The neuroscience of empathy: progress, pitfalls, and promise. *Nature Neuroscience, 15,* 675-680. doi: 10.1038/nn3085

CHAPTER 3
EFFECTS OF BEING IMITATED ON MOTOR RESPONSES EVOKED BY PAIN OBSERVATION: EXERTING CONTROL DETERMINES ACTION TENDENCIES WHEN PERCEIVING PAIN IN OTHERS[1]

Brain imaging research has shown that experiencing pain oneself and perceiving pain in others lead to a similar pattern of activation, suggesting that the latter is based on internal simulation of the observed pain. Further evidence for this idea stems from transcranial magnetic stimulation measuring corticospinal excitability (CSE). It has been demonstrated that our motor cortex is involved whenever we observe another person receiving painful stimulation to the hand (e.g. Avenanti, Bueti, Galati, & Aglioti, 2005). However, both decreases and increases of CSE have been described during pain observation. Hence the exact nature of these CSE changes has remained unclear so far. In the present study, we hypothesized that CSE changes are determined by the control that the observer has over the hand that receives painful stimulation. To test this hypothesis, we manipulated the control over the observed hand using a paradigm in which participants' movements are being imitated by a hand on screen – giving them full control over the hand – or not. In accordance with previous results, we evidenced a decrease in CSE when participants experienced no control over the hand that received painful stimulation. In contrast, inducing control resulted in an increase in CSE. We conclude that exerting control over the observed hand leads to a completely altered action tendency. Whereas an anaesthetic response is typically observed in the absence of control, increasing control induces motor facilitation reminiscent of preparation of an avoidance response.

---

[1] De Coster, L., Andres, M., & Brass, M. (2014). Effects of being imitated on motor responses evoked by pain observation: Exerting control determines action tendencies when perceiving pain in others. *Journal of Neuroscience, 34*, 6952-6957. doi: 10.1523/JNEUROSCI.5044-13.2014

INTRODUCTION

Since the study of Singer et al. (2004), it has been repeatedly shown that the observation of pain in a model results in pain-related brain activation in the observer (for a review see Lamm, Decety, & Singer, 2011). More recently, transcranial magnetic stimulation (TMS) studies have investigated how our motor system responds when perceiving pain in others. Interestingly, these studies have shown that the observation of painful stimulation delivered to the hand of a human model induces a *decrease* in corticospinal excitability (CSE) in the hand of the observer (e.g. Avenanti, Bueti, Galati, & Aglioti, 2005; Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2006). It has been argued that this inhibitory effect is similar to what happens on the motor level when experiencing pain oneself (e.g. Farina, Tinazzi, Le Pera, & Valeriani, 2003; Le Pera et al., 2001; Urban et al., 2004). However, recent findings indicate that the decrease in CSE observed while perceiving pain in others is not always found. It has been shown that this inhibition is reduced in individuals with high levels of trait-personal distress (Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2009). Furthermore, Fitzgibbon et al. (2012) have shown that pain synesthetes (i.e. individuals who experience actual pain when observing injury to another) show a significant *increase* in CSE while observing pain in others. These discrepant results raise questions about the factors that determine the nature of CSE changes induced by pain observation. A potential hypothesis is that, in experiments demonstrating an anaesthetic motor inhibition after painful stimulation, participants were unable to avoid the pain or predict the exact timing of painful stimulation (e.g. Le Pera et al., 2001; Urban et al., 2004). Similarly, in experiments where participants perceive pain in others, the decrease in CSE is typically associated with an absence of control over the hand in pain. On the other hand, high levels of personal distress or synesthetic sensations may enhance the feeling that pain is inflicted on one's own hand and

activate motor control processes, resulting in increased CSE as a reflection of planning an avoidance reaction to the observed pain. In the present study, we tested the original hypothesis that the nature of the CSE changes evoked by perceiving others' hand receiving painful stimulation is determined by our ability to exert control over this hand.

We recently manipulated the sense of control participants had over an observed hand in pain using a well-established imitation paradigm (De Coster, Verschuere, Goubert, Tsakiris, & Brass, 2013). In an imitative condition a hand on screen imitated participants, giving them perfect control over this hand. In a non-imitative condition, the hand was performing non-matching movements. We showed that affective reactions to perceiving painful stimulation in others were enhanced after being imitated by the other person and that this enhancement was related to an increase in control. In the present study, this imitation paradigm allowed us to investigate whether inducing control over the hand on screen determines whether perceiving pain in this hand will lead to increased or decreased CSE.

MATERIALS AND METHODS

Participants

Twenty-five healthy young adult men (mean age = 22.44 years, SD = 2.03) participated in the study in exchange for 40 Euros, and provided written consent beforehand. All participants had no history of neurological or psychiatric disorders, had normal or corrected-to normal vision, and were negative for the risk factors associated with TMS (Rossi et al., 2009). The procedures were non-invasive and were performed in accordance with the ethical standards laid down

in the 1964 Helsinki Declaration. The study was granted ethical approval by the Medical Ethical Review Board of Ghent University Hospital.

Experimental design

Blocks of trials consisted of two phases: an action phase in which movements of the subjects were imitated (exerting control block) or not (not exerting control block), and a pain perception phase which immediately followed the action phase. In the pain perception phase, one of ten pain movies was presented (*'bore goes into the back of the hand'*, *'hammer is smacked on the back of the hand'*, *'hot iron is pressed on the back of the hand'*, *'knife cuts the back of the hand'*, *'nail is knocked into the back of the hand with a hammer'*, *'nail of the ring finger is pulled out of the hand'*, *'paper makes a paper cut in the back of the hand'*, *'pinchers pinch the back of the hand'*, *'sandpaper is rubbed over the back of the hand'*, *'stapler puts a staple into the back of the hand'*), or a neutral movie was shown in which a still hand appeared on screen, serving as a baseline for the pain movies. Each pain movie was combined two times with both an exerting control and not exerting control block, while the neutral movie was combined 20 times with each block to ensure that an equal amount of pain and neutral movies was presented. As such, the experiment consisted of 80 trials. The association of the different pain/neutral movies with the different block conditions was completely randomized across participants.

Stimuli and apparatus

Stimulus material consisted of three types of 720 x 576 video-clips created by professionals: a hand in a resting position, simple finger movements (for the action phase of the task), and pain movies showing a hand receiving pain stimulation (for the pain movies in the pain perception phase).

During the action phase of the experimental task, participants carried out simple finger movements of the index, middle, ring, or little finger. These finger movements were recorded with a custom-built response device using light

sensors. This device allowed us to use finger lifting movements of participants as triggers for the presentation of the appropriate finger movement video. Temporal resolution was optimized (see Procedure) so that participants immediately viewed a video-taped finger movement on screen after initiating a finger movement with their own hand. For example, in an exerting control block, the lifting of an index finger resulted in the presentation of the index finger lifting video, while the middle, ring, or little finger lifting video was shown in a not exerting control block. All finger movement clips had a total duration of 2000 ms.

The perception phase of the experimental task consisted of the presentation of one of ten pain movies in which painful stimulation was applied to the hand on screen, or a resting state movie in which the right hand was displayed palm down with fingers slightly spread. The position of the video-taped hand matched the position of the participants' right hand on the response box. All movies had a total duration of 8000 ms. The resting state movie served as a neutral/baseline movie for the pain movies (Avenanti et al., 2009). Practical constraints (including timing of the experiment) detained us from using additional control conditions in which hands are innocuously touched by similar objects. While several studies have shown that CSE is modulated by observation of pain but not of touch stimuli (e.g. Avenanti et al., 2005, Avenanti, Sirigu, & Aglioti, 2010) we cannot exclude the possibility that our modulations are not specific for pain and can be extended to any hand-object interaction.

Procedure

Participants were seated in front of a standard computer screen at arm length, and asked to place the four fingers of their right hand on a custom-made response box. Display of stimulus material and recording of responses were conducted with Presentation software (Neurobehavioral Systems, Inc.). As soon as the video-taped right hand appeared on screen (resting state movie), subjects were instructed to voluntary move a randomly chosen finger that was placed on

the response box. Immediately after movement of one of the subjects' fingers (delay = 0 ms, estimate of intrinsic delay of computer/software = 66.93 ms), a movie was shown in which the hand on screen performed the same or a different movement for exerting control and not exerting control blocks respectively. After a random number between 10 and 15 of such movements (all imitative or all non-imitative), one of the pain movies or the neutral movie was immediately presented. After a pain movie, participants had to rate the behavioural statement 'I felt pain on my own hand when I saw the hand on screen receiving painful stimulation' on a scale from -5 to +5. During the pain movies, a TMS pulse was applied at the exact time when the painful tool contacted the skin surface. During the neutral movie, the TMS pulse was delivered at 2900 ms, corresponding to the average of the TMS pulse onset across all pain movies.

Before the start of the experiment, participants' TMS motor threshold was measured as described in the TMS and Electromyography paragraph below. Afterwards, they performed two practice blocks (both an exerting control and a not exerting control block), in which a pain movie was shown that was not used during the experimental phase and no TMS pulse was applied. During these practice blocks, it was verified whether participants understood all aspects of the experimental procedure.

Finally, at the end of the experiment, participants filled in the Interpersonal Reactivity Index (IRI; Davis, 1980; for Dutch translation see De Corte et al., 2007), used as a measure of trait empathy. This questionnaire consists of 28 items which have to be rated on a 5-point Likert scale, and can be divided into four subscales: Perspective Taking (PT, the tendency to spontaneously imagine and assume the cognitive perspective of another person), Empathic Concern (EC, the tendency to feel sympathy and compassion for others in need), Fantasy (FS, the tendency to project oneself into the place of fictional characters in books and movies), and Personal Distress (PD, the extent to which an individual feels

distress as a result of witnessing another's emotional distress). Cronbach's α in the current study for PT was .83, for EC .74, for FS .79, and for PD .80.

TMS and electromyography

Single pulse TMS was delivered through a biphasic magnetic stimulator (Rapid^2 Magstim, Whitland, UK) connected to a polyeruthane-coated figure-of-eight coil (5.4-cm inner diameter windings). The coil was held tangentially over the left hand motor area, with the handle pointing backwards and forming an angle of 45° with the sagittal plane. Participants wore earplugs to attenuate the coil noise. Electromyographical (EMG) activity was recorded with the ActiveTwo system (BioSemi, Amsterdam, The Netherlands). Sintered 11 x 17-mm active Ag–AgCl electrodes were placed over the right First Dorsal Interosseus muscle (FDI) and the right Brachioradialis muscle (BR) in a belly–tendon arrangement. The FDI contributes to flex or abduct the index away from the middle finger, whereas the main action of the BR is to flex the forearm at the elbow. These muscles were chosen because they are involved, respectively, in finger and hand retraction, two reactions commonly observed in response to painful stimuli as used in our study. The hot spot in the hand motor area was established by locating a stimulation site where TMS elicited motor evoked potentials (MEPs) in the two muscles. TMS intensity was set at 110 % of the resting motor threshold, i.e. the minimum intensity to induce an MEP $\geq$ 50 μV peak to peak in both muscles with 50 % probability. In 14 out of 25 participants, the TMS parameters were defined according to the FDI only because it was not possible to elicit MEPs in both muscles from the same stimulation site. The data collected from the BR in other participants were excluded from further analyses because the number of trials where an MEP was observed during the experiment was too small. Average intensity (± S.D.) was 71.25 (± 16.98) % of the maximal stimulator output. EMG signal was amplified (internal gain scaling), digitized at 2 kHz, high-pass filtered at 3 Hz, and stored on a PC for off-line analysis.

Data analyses

Trials were excluded when the root mean square (RMS) of the background EMG signal recorded in the FDI 500 ms before TMS was higher than 50 μV. For each subject, the top and bottom 5% of MEPs were trimmed and the peak-to-peak amplitude of the remaining MEPs was computed using Matlab. For both control conditions separately, the MEPs in each pain condition were expressed as a percentage of change with respect to its corresponding baseline as follows: 100 * (Pain – Neutral)/Neutral. The baseline conditions did not differ significantly from each other, $t(24) = 1.34$, $p = .20$.

Planned comparisons between exerting control and not exerting control over the observed hand were performed for behavioural and TMS data using paired *T*-tests. For the latter, additional analyses were performed to rule out that the effects described in the Results section were due to differences in background EMG activity. These analyses showed that our manipulation did not influence the RMS of the EMG signal recorded from the FDI during a 500 ms delay before the TMS (all *p*-values >.20).

Pearson correlations were computed between the average ratings on each subscale of the IRI and the percentage of change in MEP amplitude in the exerting control and not exerting control conditions. One outlier participant was identified using Cook's distance and subsequently removed from the correlation analysis.

RESULTS

Subjective Reports

In accordance with previous results (De Coster et al., 2013), a paired *T*-test revealed that scores were significantly higher in the exerting control compared to the not exerting control condition: $t(24) = 2.31$, $p < .05$, $d = .15$ (see Figure 1).

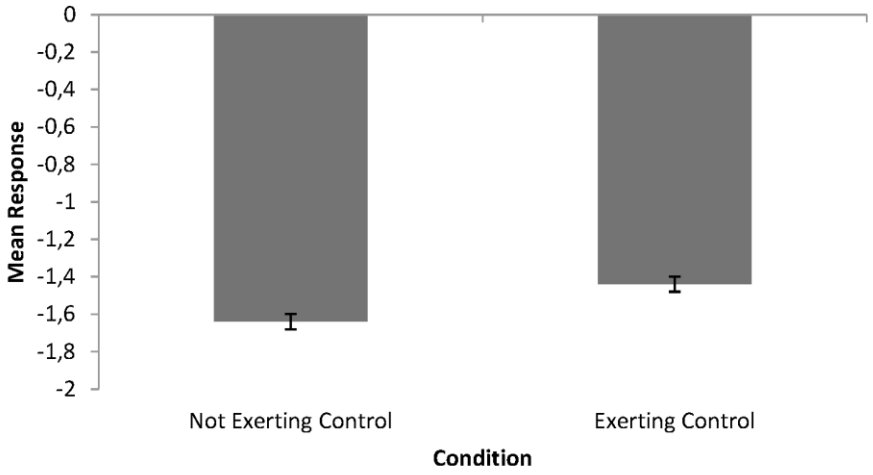


Figure 1: Mean scores on the question *'I felt pain on my own hand when I saw the hand on screen receiving painful stimulation'* (range from -5 to +5) in the exerting control and not exerting control condition after observing a pain movie. Error bars are standard errors of the mean.

TMS data

Planned comparisons of the percentage of change in MEP amplitude in the FDI showed a significant difference between the exerting control and not exerting control condition: $t(24) = 3.44$, $p < .01$, $d = 1.87$. As shown in Figure 2, MEP

amplitude decreased in the not exerting control condition (one –sample *T*-test against 0: $t(24) = -2.29$, $p < .05$, $d = .93$), replicating previous findings (e.g. Avenanti et al., 2005, 2006). In contrast, MEP amplitude increased in the exerting control condition (one –sample *T*-test against 0: $t(24) = 2.63$, $p < .05$, $d = 1.07$).

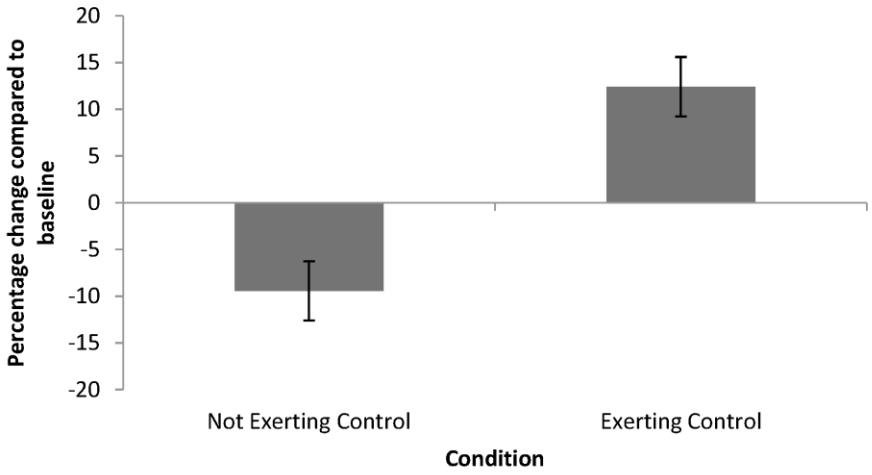


Figure 2: Mean CSE in the exerting control and not exerting control, computed as the percentage change compared to baseline [100 * (Pain – Neutral)/Neutral]. Error bars are standard errors of the mean.

Correlations were computed between the average rating of each subscale of the IRI and the percentage of change in MEP amplitude, averaged for the exerting control and not exerting control condition separately. A negative relationship was found between PT and MEP amplitude in the not exerting control condition ($r = -.60$, $p < .01$; see Figure 3a). In other words, participants who were more likely to cognitively infer others' states showed a stronger inhibition at the motor level. Furthermore, a positive relationship was found between PD and MEP amplitude

in the exerting control condition (r = .53, p < .01; see Figure 3b), meaning that participants who were more likely to feel distressed about seeing someone else suffering showed a stronger motor facilitation. No other correlations were found between subscales of the IRI and the change in MEP amplitude in the exerting or not exerting control condition (all ps > .05).

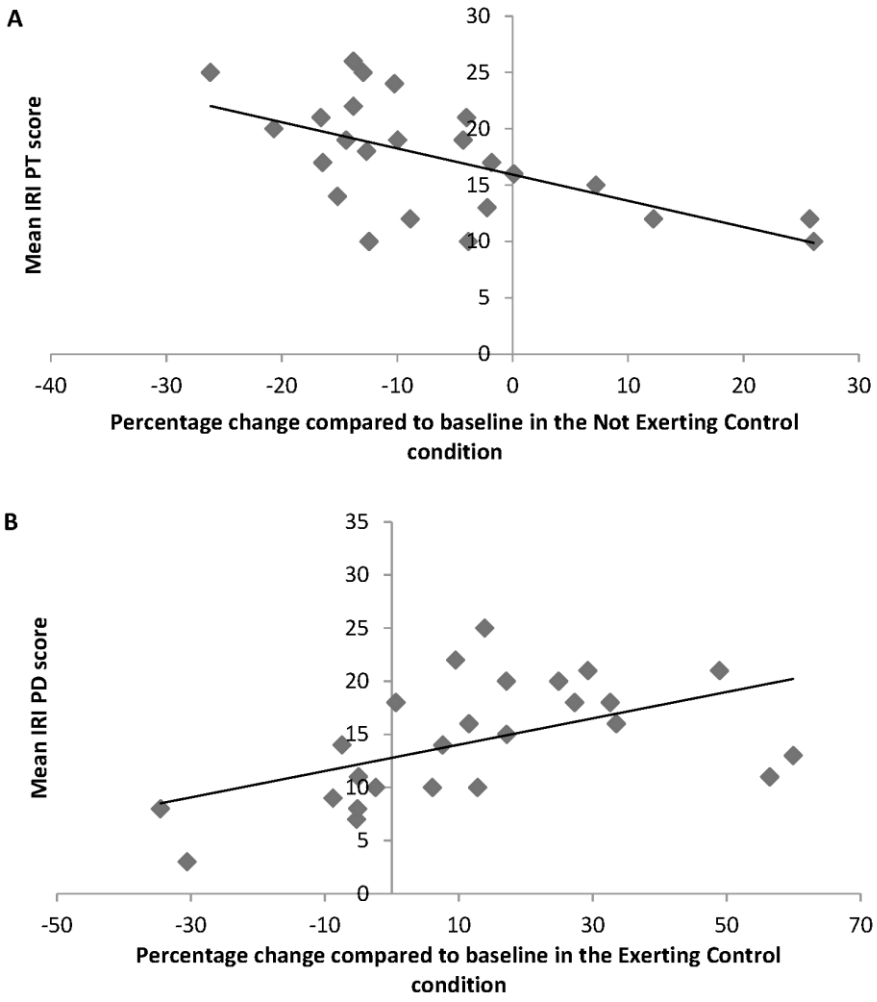


Figure 3: A. Correlation between mean IRI Perspective Taking (PT) score and mean CSE in the not exerting control condition. B. Correlation between mean IRI Personal Distress (PD) score and mean CSE in the exerting control condition.

DISCUSSION

In this TMS experiment, we investigated whether action tendencies evoked by painful stimuli delivered to the hand of a human model depend on the ability to exert control over the observed hand. Subjects observed the hand of another person receiving painful stimulation, after being imitated by this hand or not. During the pain perception phase, TMS-induced MEPs were measured in the right dominant hand of participants. In accordance with previous results, we showed that when participants did not exert control over the hand that received painful stimulation (i.e. incongruent movements), decreased CSE was found during pain observation. By contrast, when participants exerted control over the hand that received painful stimulation (i.e. congruent movements), increased CSE was observed.

It has been repeatedly shown that observing others in pain does not only generate affective but also sensory-motor responses in the observer (Keysers, Kaas, & Gazzola, 2010; Lamm et al., 2011). Indeed, several TMS studies exploring reactions to perceiving pain in others evidenced decreased excitability in the motor system of the observer. This decrease has been shown to be specific to the body part that was hurt in others and to correlate with the pain intensity as estimated by the observer (e.g. Avenanti et al., 2005, 2006; Minio-Paluello, Avenanti, & Aglioti, 2006). It has been argued that this inhibition reflects a freezing response that is similar to the reaction observed when actually experiencing pain (e.g. Farina et al., 2003; Le Pera et al., 2001; Urban et al., 2004). Other research, however, has shown that high levels of personal involvement are associated with reduced motor inhibition during pain observation (Avenanti et al., 2009). Moreover, Fitzgibbon et al. (2012) have shown that pain synesthetes show a significant increase of CSE when observing someone else in pain. The current study accounts for these discrepancies by showing that action

tendencies are modulated by the level of control participants exerted over the hand that received painful stimulation.

Several TMS studies have shown that increased CSE might reflect anticipatory changes to perception of negative emotional cues (Oliveri et al., 2003; Koganemaru, Domen, Fukuyama, & Mima, 2012; Borgomaneri, Gazzola, & Avenanti, 2013). Furthermore, it has been shown that the motor system implements anticipatory simulations of expected actions (Avenanti, Annella, Candidi, Urgesi, & Aglioti, 2013; Borroni, Montagna, Cerri, & Baldissera, 2005; Kilner, Vargas, Duval, Blakemore, & Sirigu, 2004; Urgesi et al., 2010). We assume that the facilitation of CSE observed in the exerting control condition reflects planning of an avoidance reaction to the observed pain. In particular, this increased CSE might reflect an unspecific muscle tension halting ongoing behaviour in order to prepare for a potential avoidance response. Such an avoidance response is only adaptive when the agent has the possibility to escape the painful stimulation. Previous studies examining CSE when experiencing pain oneself used methods (e.g. saline injection, electrical stimulation) that prevent preparation of appropriate reactions to avoid pain (e.g. Le Pera et al., 2001; Urban et al., 2004). In such situations where it is already too late to stop or avoid the painful stimulation, an anaesthetic motor inhibition is the most adaptive response. By definition, situations in which participants passively observe pain to the hand of a human model preclude an active avoidance response, and thus anaesthetic motor inhibition is displayed. In a previous study, De Coster et al. (2013) showed a reduced sense of agency when the hand that receives pain does not imitate the finger movements executed by participants. In this sense, the "not exerting control" condition is similar to observing others in pain without any possibility to prepare an avoidance reaction to this pain. In support of this view and in line with previous research (Avenanti et al., 2009; Avenanti et al., 2010; Minio-Paluello, Baron-Cohen, Avenanti, Walsh, & Aglioti, 2009), a correlation was found in our

study between this inhibitory effect and the individual ratings of perspective taking, a cognitive marker of empathy, in the not exerting control condition. It seems that the more a participant feels able to cognitively change his/her perspective to adopt others' point of view, the more he/she experiences motor inhibition during pain observation. Interestingly, Shamay-Tsoory, Aharon-Peretz, and Perry (2009) suggested that perspective taking is closely related to Theory of Mind abilities and the awareness that others' states are different from one's own. By contrast, being imitated provides participants with a feeling of control over the model hand, due to an increased self-other overlap (De Coster et al., 2013). The more participants are distressed about seeing the hand that they can control, the more they show activation in this hand. This correlation is in accordance with Borgomaneri et al. (2013) who found that inter-individual differences in personal distress were positively correlated with an increased CSE. Interestingly, facilitory CSE responses when viewing negative stimuli seem to be muscle unspecific (e.g. Borgomaneri et al., 2013). This raises the possibility that facilitation of CSE might be part of a more generalized preparatory response towards negative situations, especially since Borgamaneri et al. (2013) indicated the very early nature of these facilitory responses. This might indicate that the first response to a threatening situation is a complete and unspecific muscle tension that serves the role of stopping ongoing behaviour and preparing avoidance. Unfortunately, we were not able to test this hypothesis because the data from the only other muscle we measured (the BR muscle) were not reliable.

In accordance with previous results (De Coster et al., 2013), we showed that behavioural self-reports of pain intensity were higher in the exerting control condition compared to the not exerting control condition. Furthermore, in this previous study both other- and self-oriented feelings were rated higher in the exerting control condition, reflecting concern and personal distress respectively (Batson, Fultz, & Schoenrade, 1987). In addition, we found that not only

agency/control was higher in the imitation condition, but that this condition elicited higher body ownership as well. In particular, we demonstrated that exerting control induced a rubber hand illusion (RHI) indicating enhanced body ownership (De Coster et al., 2013). It is therefore an open question whether the effect of exerting control directly influenced the action tendency or whether this effect is mediated by increased body ownership. In any case, our study is the first experimental study showing increased CSE in a situation where self-other overlap is high. While it has been shown using fMRI that threatening a rubber hand that feels as if it is your own hand increases brain activity in pain-related and motor-related areas (Ehrsson, Wiech, Welskopf, Dolan, & Passingham, 2007), the specific nature of the motor response (inhibition or facilitation) cannot be investigated with fMRI. Interestingly, other research (Schütz-Bosbach, Mancini, Aglioti, & Haggard, 2006; Schütz-Bosbach, Avenanti, Aglioti, & Haggard, 2009) has shown that when applying motor TMS in a RHI paradigm (without observation of noxious stimulation), differential modulation of the FDI was present as well. While asynchronous stimulation (no RHI) led to increased MEP amplitude and reduced cortical silent period duration when observing index finger movements, synchronous stimulation (RHI) led to the opposite pattern. These results confirm the idea that self-other overlap can modulate CSE, reflecting appropriate responses to the observed stimuli.

In addition, our study provides the first systematic evidence that CSE changes induced by pain observation are mediated by the merging of self-other representations. Although it has been widely accepted that the inhibitory effect is due to an embodiment of the observed pain, this has never been systematically demonstrated. With the current paradigm we demonstrated that CSE effects in the "exerting control" condition are qualitatively different from those in the "not exerting control" condition. Our study thus suggests that increasing self-other overlap (due to being imitated in the "exerting" condition) leads to a facilitation

of MEPs when observing pain, and that this facilitation is higher for people who are more strongly affected by other's distress. As such, these results indicate that being imitated has a strong influence both on emotional reactions, such as empathy for pain, and bodily reactions in the observer. Enhancing self-other overlap by being imitated thus provides a novel and original paradigm for investigating pathological populations, such as autism or schizophrenic individuals, who show altered emotional reactions that are related to deficiencies in self-other representations (e.g. autism, schizophrenia).

In sum, our results indicate that whether we exert control over an observed body part or not determines the nature of the CSE changes consecutive to perceiving pain in others. While having no control leads to motor inhibition when observing someone in pain, exerting control leads to motor facilitation. We argue that this increase in CSE response reflects the tendency to prepare for avoidance of the painful stimulation. By contrast, having no control over the hand rather elicits an anaesthetic response, as evidenced by motor inhibition.

REFERENCES

Avenanti, A., Annella, L., Candidi, M., Urgesi, C., & Aglioti, S. M. (2013). Compensatory plasticity in the action observation network: virtual lesions of STS enhance anticipatory simulation of seen actions. *Cerebral Cortex, 23*, 570-580. doi: 10.1093/cercor/bhs040

Avenanti, A., Bueti, D., Galati, D., & Aglioti, S. M. (2005). Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nature Neuroscience, 8*, 955-960. doi: 10.1038/m1481

Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2006). Stimulus-driven modulation of motor-evoked potentials during observation of others' pain. *Neuroimage, 32*, 316-324. doi: 10.1016/j.cortex.2008.10.004

Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2009). The pain of a model in the personality of an onlooker: Influence of state-reactivity and personality traits on embodied empathy for pain. *Neuroimage, 44*, 275-283. doi: 10.1016/j.neuroimage.2008.08.001

Avenanti, A., Sirigu, A., & Aglioti, S. M. (2010). Racial bias reduces empathic sensorimotor resonance with other-race pain. *Current Biology, 20*, 1018-1022. doi: 10.1016/j.cub.2010.03.071

Batson, C. D., Fultz, J., & Schoenrade, P. A. (1987). Distress and empathy – 2 qualitatively distinct vicarious emotions with different motivational consequences. *Journal of Personality, 55*, 19-39. doi: 10.1111/j.1467-6494.1987.tb00426.x

Borgomaneri, S., Gazzola, V., & Avenanti, A. (2013). Temporal dynamics of motor cortex excitability during perception of natural emotional scenes. Social Cognitive and Affective Neuroscience. doi: 10.1093/scan/nst139

Borroni, P., Montagna, M., Cerri, G., & Baldissera, F. (2005). Cyclic time course of motor excitability modulation during the observation of a cyclic hand movement. *Brain Research, 1065*, 115-124. doi: 10.1016/j.brainres.2005.10.034

Davis, M. H. (1980). A multidimensional approach to individual differences in empathy. *JSAS Catalog of Selected Documents in Psychology, 10*, 85.

De Corte, K., Buysse, A., Verhofstadt, L. L., Roeyers, H., Ponnet, K., & Davis, M. H. (2007). Measuring empathic tendencies: reliability and validity of the Dutch version of the Interpersonal Reactivity Index. *Psychologica Belgica, 47*, 235-260.

De Coster, L., Verschuere, B., Goubert, L., Tsakiris, M., & Brass, M. (2013). I suffer more from your pain when you act like me: Being imitated enhances affective responses to seeing someone else in pain. *Cognitive, Affective, & Behavioral Neuroscience, 13*, 519-532. doi: 10.3758/s13415-013-0168-4

Ehrsson, H. H., Wiech, K., Welskopf, N., Dolan, R. J., & Passingham, R. E. (2007). Threatening a rubber hand that you feel is yours elicits a cortical anxiety response. *Proceedings of the National Academy of Sciences in the United States of America, 104*, 9828-9833, doi: 10.1073/pnas.0610011104

Farina, S., Tinazzi, M., Le Pera, D., & Valeriani, M. (2003). Pain-related modulation of the human motor cortex. *Neurological Research, 25*, 130-142. doi: 10.1179/016164103101201283

Fitzgibbon, B. M., Enticott, P. G., Bradshaw, J. L., Giummarra, M. J., Chou, M., Georgiou-Karistianis, N., & Fitzgerald, P. B. (2012). Enhanced corticospinal response to observed pain in pain synesthetes. *Cognitive, Affective, & Behavioral Neuroscience, 12*, 406-418. doi: 10.3758/s13415-011-0080-8

Keysers, C., Kaas, J. H., & Gazzola, V. (2010). Somatosensation in social perception. *Nature Reviews Neuroscience, 11*, 417-428. doi: 10.1038/nrn2833

Kilner, J. M., Vargas, C., Duval, S., Blakemore, S. J., & Sirigu, A. (2004). Motor activation prior to observation of a predicted movement. *Nature Neuroscience, 7*, 1299-1301. doi: 10.1038/nn1355

Koganemaru, S., Domen, K., Fukuyama, H., & Mima, T. (2012). Negative emotion can enhance human motor cortical plasticity. *European Journal of Neuroscience, 35*, 1637-1645. doi: 10.1111/j.1460-9568.2012.08098.x

Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage, 54*, 2492-2502. doi: 10.1016/j.neuroimage.2010.10.014

Le Pera, D., Graven-Nielsen, T., Valeriani, M., Oliviero, A., Di Lazzaro, V., & Tonali, P. A. (2001). Inhibition of motor system excitability at cortical and spinal level by tonic muscle pain. *Clinical Neurophysiology, 112*, 1633-1641. doi: 10.1016/S1388-2457(01)00631-9

Minio-Paluello, I., Avenanti, A., & Aglioti, S. M. (2006). Left hemisphere dominance in reading the sensory qualities of others' pain? *Social Neuroscience, 1*, 320-333. doi: 10.1080/17470910601035954

Minio-Paluello, I., Baron-Cohen, S., Avenanti, A., Walsh, V., & Aglioti, S. M. (2009). Absence of embodied empathy during pain observation in Asperger Syndrome. *Biological Psychiatry, 65*, 55-62. doi: 10.1016/j.biopsych.2008.08.006

Oliveri, M., Babiloni, C., Filippi, M. M., Caltagirone, C., Babiloni, F., Cicinelli, P., Traversa, R., Palmieri, M. G., & Rossini, P. M. (2003). Influence of the supplementary motor area on primary motor cortex excitability during movements triggered by neutral or emotionally unpleasant visual cues. *Experimental Brain Research, 149*, 214-221. doi: 10.1007/s00221-002-1346-8

Rossi, S., Hallet, M., Rossini, P. M., Pascual-Leone, A., and the Safety of TMS consensus group. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology, 120*, 2008-2039. doi: 10.1016/j.clinph.2009.08.016

Schütz-Bosbach, S., Avenanti, A., Aglioti, S. M., & Haggard, P. (2009). Don't do it! Cortical inhibition of self-attribution during action observation. *Journal of Cognitive Neuroscience, 21*, 1215-1227. doi: 10.1162/jocn.2009.21068

Schütz-Bosbach, S., Mancini, B., Aglioti, S. M., & Haggard, P. (2006). Self and other in the human motor system. *Current Biology, 16*, 1830-1834. doi: 10.1016/j.cub.2006.07.048

Shamay-Tsoory, S. G., Aharon-Peretz, J., & Perry, D. (2009). Two systems for empathy: a double dissociation between emotional and cognitive empathy in inferior frontal gyrus versus ventromedial prefrontal lesions. *Brain, 132*, 617-627. doi: 10.1093/brain/awn279

Singer, T., Seymour, B., O'Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for pain involves the affective but not sensory components of pain. *Science, 303*, 1157-1162. doi: 10.1126/science.1093535

Urban, P. P., Solinski, M., Best, C., Rolke, R., Hopf, H. C., & Dieterich, M. (2004). Different short-term modulation of cortical motor output to distal and proximal upper-limb muscles during painful sensory nerve stimulation. *Muscle & Nerve, 29*, 663-669. doi: 10.1002/mus.20011

Urgesi, C., Maieron, M., Avenanti, A., Tidoni, E., Fabbro, F., & Aglioti, S. M. (2010). Simulating the future of actions in the human corticospinal system. *Cerebral Cortex, 20*, 2511-2521. doi: 10.1093/cercor/bhp292

CHAPTER 4
AN FMRI STUDY ON THE INFLUENCE OF BEING IMITATED ON EMPATHY FOR PAIN[1]

Being imitated has been shown to have several positive social consequences. In a recent study, it was shown that being imitated does not only affect complex social behaviour, but that it influences a basic process such as empathy for pain as well. Empathy for pain refers to the idea that pain-related brain activation is found when observing someone else in pain. In a paradigm designed to investigate the influence of being imitated on empathy for pain, participants' finger movements are being imitated by a hand on screen or not. Subsequently, the hand on screen receives painful stimulation. In the current fMRI study, brain activation was measured to investigate which brain areas related to pain observation are modulated by being imitated. Furthemore, it was explored whether neural evidence was found for the idea that self-other overlap underlies this effect. Peak activity was found in the right dorsal anterior insula (AI), supporting the idea that being imitated enhances activation in pain-related brain areas. Interestingly, this region has been related to translation of affective states into action tendencies. Furthermore, activation was found in the right temporo-parietal junction (TPJ), a region associated with self-other distinction. This activity was positively correlated with activation in the AI, indicating that stronger affective responding was associated with a greater need for distinction between self and other. These results provided the first direct evidence for the idea that being imitated modulates empathy for pain, and support a shared representational account.

[1]De Coster, L., Desmet, C., Demanet, J., Goubert, L., & Brass, M. (in preparation). An fMRI study on the influence of being imitated on empathy for pain.

INTRODUCTION

Imitation is important for our daily social interactions, changing the way we experience others. Research has indicated that being imitated elicits positive social behaviour towards others (Kühn et al., 2010; Lakin, Chartrand, &Arkin, 2008; Stel, van Baaren, & Vonk, 2008). Chartrand and Bargh (1999), for example, have shown that we like someone who imitates us more, and that interactions with this person run more smoothly (Chameleon effect). This raises the question whether being imitated also affects more basic social-cognitive processes such as empathy for pain. In her seminal study, Singer et al. (2004) showed that perceiving another person in pain activates brain regions involved in the affective–motivational dimensions of pain (see also Goubert, Vervoort, & Craig, 2012; Jackson, Meltzoff, & Decety, 2005; Lamm, Decety, & Singer, 2011; Singer et al., 2006). Originally thought that this phenomenon, called empathy for pain, only comprised the affective part of the pain matrix (including areas such as the anterior insula, AI and anterior cingulate cortex, ACC), research has since then shown that sensory sharing takes place as well (for a review see Keysers, Kaas, & Gazzola, 2010, for a meta-analysis see Lamm et al., 2011). Moreover, research has indicated that sharing of representations when observing someone else in pain is modulated both by top-down mechanisms (e.g. Cheng et al., 2007; Decety, Echols, & Corell, 2009; de Vignemont & Singer, 2006; Hein & Singer, 2008; Lamm, Meltzoff, & Decety, 2010; Singer et al., 2006), and bottom-up features (e.g. Han, Fan, & Mao, 2008; Yang, Decety, Lee, Chen, & Cheng, 2009; Xu, Zuo, Wang, & Han, 2009), suggesting that both factors contribute to the empathic response (Decety & Lamm, 2006). The general aim of the current study was to investigate the

role of being imitated on brain activation when observing someone else in pain.

In a recent study, De Coster, Verschuere, Goubert, Tsakiris, & Brass (2013) were able to show that observing someone else in pain is influenced by being imitated due to increased self-other merging. In this experiment, subjects were imitated by a hand on screen or not, and subsequently saw this hand receiving painful stimulation. During this pain perception phase, affective responses were higher when previously being imitated. Furthermore, a second experiment indicated that this effect was mediated by increased self-other merging. In a transcranial magnetic stimulation (TMS) study, it was shown that action tendencies were differentially affected by the imitation manipulation (De Coster, Andres, & Brass, 2014), suggesting that bodily reactions when observing pain can be influenced by self-other overlap via an imitation manipulation.

In the current study, we used the aforementioned paradigm to investigate which brain regions are active when observing someone else in pain after being imitated. Investigating the influence of being imitated on brain activation during pain perception allows us to address two fundamental questions. First, we could investigate which part of the pain matrix is more strongly activated when empathy for pain is modulated by being imitated. Secondly, it was possible to provide neural evidence for the idea that self-other overlap might underlie the effect. As mentioned above, it was suggested in De Coster et al. (2013) that increased self-other merging mediates the effect of being imitated on empathy for pain. Based on previous imaging work on self-other distinction it could be predicted that the temporo-parietal junction is involved (TPJ, Brass, Ruby, & Spengler, 2009; Spengler, von Cramon, & Brass, 2010). Thus, the current study allowed us to

additionally test the hypothesis that manipulation of being imitated modulates activation in the TPJ.

MATERIALS AND METHODS

Participants

Nineteen healthy female volunteers (mean age = 23 years, SD = 3.04) participated in the study in exchange for 29 Euros. One participant was excluded from analyses due to inability to perform the task adequately. All participants were right handed as measured by the Edinburgh Inventory (Oldfield, 1971). They provided written consent beforehand and had no history of neurological disorders. Ethical approval was granted by the Medical Ethical Review Board of the Ghent University Hospital.

Experimental design

Trials consisted of two phases: an action phase in which movements of the subjects were imitated or not, and a pain perception phase which immediately followed the action phase. In the pain perception phase, one of ten pain movies (*'bore goes into the back of the hand', 'hammer is smacked on the back of the hand', 'hot iron is pressed on the back of the hand', 'knife cuts the back of the hand', 'nail is knocked into the back of the hand with a hammer', 'nail of the ring finger is pulled out of the hand', 'paper makes a paper cut in the back of the hand', 'pinchers pinch the back of the hand', 'sandpaper is rubbed over the back of the hand', 'stapler puts a staple into the back of the hand'*), or one of two neutral movie was presented (*'cue tip is rubbed on the back of the hand', 'cotton-wool is rubbed on the back of the hand'*). Seven pain movies were chosen randomly per subject, which ensured that nine different movies were shown. Each movie was presented

four times with both an imitation and a non-imitation trial, resulting in a total amount of 72 trials, divided into two parts of 36 trials.

Stimuli and apparatus

Display of stimulus material and recording of responses were conducted with Presentation software (Neurobehavioral Systems, Inc.). Stimulus material consisted of three types of 720 x 576 video-clips created by professionals: a hand in a resting position, simple finger movements (for the action phase of the task), and pain movies showing a hand receiving pain stimulation or neutral movies showing a hand receiving non-painful stimulation (for the movies in the pain perception phase).

During the action phase of the experimental task, participants carried out simple finger movements of the index, middle, ring, or little finger. These finger movements were recorded with an fMRI-compatible response box. Participants were instructed to press one of four buttons with one of their four fingers, and perform a finger lifting movement immediately afterwards. Temporal resolution was optimized so that participants immediately viewed a video-taped finger movement on screen after pressing a response button and performing the lifting movement with their own hand. For example, in an imitation block, the pressing of the response button with and lifting of the index finger resulted in the presentation of the index finger lifting video, while the middle, ring, or little finger lifting video was shown in a non-imitation block. All finger movement clips had a total duration of 2000 ms.

The perception phase of the experimental task consisted of the presentation of a pain/neutral movie in which painful/non-painful stimulation was applied to the hand on screen. The position of the video-taped hand matched the position of the participants' right hand on the response box. All movies had a total duration of 8000 ms.

Procedure

Participants were lying in the scanner while attentively performing the task and watching the movies. As soon as a video-taped right hand appeared on screen (resting position movie), subjects were instructed to voluntary move a randomly chosen finger that was placed on the response box by pressing the response button and making a lifting movement immediately afterwards. After pressing the response button, a movie was shown in which the hand on screen performed the same or a different movement for imitation and non-imitation blocks respectively. After a random number between 10 and 15 of such movements (all imitative or all non-imitative), one of the pain or neutral movies was immediately presented. After pain movies only, participants had to rate the behavioural statements *'How unpleasant do you think the other person found the pain stimulation?'* (other-affective), *'How intense do you think the other person experienced painful sensations?'* (other-sensory), *'How unpleasant did you find the pain stimulation yourself?'* (self-affective), and *'How intense did you experience painful sensations yourself?'* (self-sensory) on a scale from -5 to +5. After responding to this last question, a new trial started. Jitters were introduced between the action phase and pain perception phase, between the pain perception phase and rating of the behavioural questions, and at the end of the trial. A pseudo logarithmic jitter was applied for all jitters. Half of the intertrial intervals were short (range between 200-2000 ms in steps of 600ms), one third were intermediate (range between 2600 ms and 4400 ms) and one sixth was long (range between 5000 ms and 6800 ms) with a mean intertrialinterval of 2700 ms. A short break was inserted in the middle of the experiment.

Before the start of the experiment, participants performed two practice blocks (both an imitation and a non-imitation block) outside of the

scanner, in which a pain movie was shown that was not used during the experimental phase. During these practice blocks, subjects were made aware of the procedure in the scanner, and it was verified whether they understood all aspects of the experimental procedure.

Image acquisition and statistical analysis

MRI images were acquired with a 3T scanner (Siemens Trio) combined with a 32-channel radiofrequency head coil. Subjects were entered head first and supine into the magnet bore. Scanning started with 176 high-resolution anatomical images using a T1-weighted 3D MPRAGE sequence ([repetition time (TR) = 2530 ms, echo time (TE) = 2.58 ms, image matrix = 256 x 256, field of view (FOV) = 220 mm, flip angle = 7°, slice thickness = 0.90 mm, voxel size = 0.9 x 0.86 x 0.86 mm (resized tot 1 x 1 x 1 mm)]. Next, two runs of whole-brain functional images were conducted using a T2*-weighted echo planar imaging (EPI) sequence, sensitive to BOLD contrast (TR = 2000 ms, TE = 35 ms, image matrix = 64 x 64, FOV = 224 mm, flip angle = 80°, slice thickness = 3.0 mm, distance factor = 17 %, voxel size = 3.5 x 3.5 x 3 mm, 30 axial slices). The amount of EPI images depended upon the self-paced speed of subjects during the trials, namely speed of finger movement execution and rating of self-reports.

All data were analyzed using SPM8 (Wellcome Department of Imaging Neuroscience, UCL, London, U.K.; http://www.fil.ion.ucl.ac.uk/spm). In order to account for T1 relaxation effects, each EPI sequence started with four dummy scans. First, all functional images were spatially realigned using rigid body transformation. After realignment, images were slice time corrected using with respect to the middle acquired slice. The structural image of each subject was co-registered with their mean functional image. Further, all functional images were normalized based on the T1-derived normalization parameters. Finally, the

images were resampled into 3.5 mm^3 voxels and spatially smoothed with a Gaussian kernel of 8 mm (full-width at half maximum).

A high pass filter of 128 s was applied during fMRI data analysis. Statistical analyses were performed using the general linear model implemented in SPM8. One model was created for the imitation phase and the pain perception phase. First, the imitation phase was modeled by looking at activation related to being imitated. For this phase, we modeled the canonical hemodynamic response function (HRF) during the entire imitation phase. The duration of this phase was dependent on the speed of participants' finger movements, of which 10 to 15 were required. Second, the activation during pain observation was modeled. The HRF was modeled at the time point when the tool with which painful/non-painful stimulation was applied appeared on screen. The model included regressors for Action condition (Imitation vs. Nonimitation) and Perception condition (Pain vs. Neutral), and an additional twelve regressors (six for each run) to control for residual head movements artifacts. Contrast images of interest were computed at first level by comparing parameter estimates for the canonical HRF. These contrast images were then entered into a second level analysis using one-sample T-tests. We will focus on clusters that were significant ($p < .05$, corrected) as calculated by SPM8 after applying a whole brain uncorrected threshold of $p < .001$.

RESULTS

Subjective reports

Except for the first question referring to unpleasant feelings of the other person, all subjective reports resulted in higher ratings after being

imitated compared to not being imitated (see Table 1); paired $t(17) = 2.12$, $p < .05$, $d = .16$; $t(17) = 2.49$, $p < .05$, $d = .32$; $t(17) = 3.05$, $p < .01$, $d = .61$ for the questions referring to other-sensory, self-affective, and self-sensory aspects respectively.

Table 1: Four behavioural questions, the aspect of empathy for pain they refer to, and their corresponding mean scores (standard deviations) in the different conditions (range from -5 to +5).

Question	Aspect	Imitation	Non-imitation
'How unpleasant do you think the other person found the pain stimulation?'	Other – affective	3.43 (1.89)	3.45 (1.89)
'How intense do you think the other person experienced painful sensations?'	Other – sensory	3.55 (1.49)	3.43 (1.44)
'How unpleasant did you find the pain stimulation yourself?'	Self – affective	2.58 (1.80)	2.27 (1.90)
'How intense did you experience painful sensations yourself?'	Self – sensory	1.30 (1.91)	.65 (2.13)

fMRI results

Whole-brain contrasts were computed to examine brain activation related to being imitated, and observing someone else in pain (after being imitated) in the action and pain perception phase respectively. To this aim, we subtracted brain activity in the Nonimitation condition from the Imitation condition in the action phase. Furthermore, we calculated Pain – Neutral in the pain perception phase to look at the main effect of pain observation.

Finally, the interaction was calculated as [(PainImitation) – (PainNonimitation) – (NeutralImitation) – (NeutralNonimitation)]. A complete list of activations is shown in Table 2.

Table 2: MNI coordinates of whole-brain contrasts.

	Peak coordinates	Z-score	Cluster size
Action phase			
Being imitated – not being imitated			
Superior temporal sulcus	51, -45, 15	5.62	29
Pain perception phase			
Pain - neutral			
Anterior medial cingulate cortex	0, 18, 33	4.21	153
Bilateral inferior frontal gyrus	57, 12, 33	6.18	306
	-57, 9, 36	6.78	192
Superior parietal lobe/precuneus	12, -54, 75	9.73	443
Amygdala	30, 3, -15	6.58	61
Occipital lobe	-48, -66, 6	17.50	5437
(PainImitation – PainNonimitation) – (NeutralImitation – NeutralNonimitation)			
Right dorsal anterior insula	30, 15, 6	5.69	63
Right temporo-parietal junction	57, -42, 24	5.29	110

In the action phase, the contrast looking at activation for being imitated was found in the right superior temporal sulcus (STS; 51, -45, 15, *z* = 5.62; see Figure 1A).

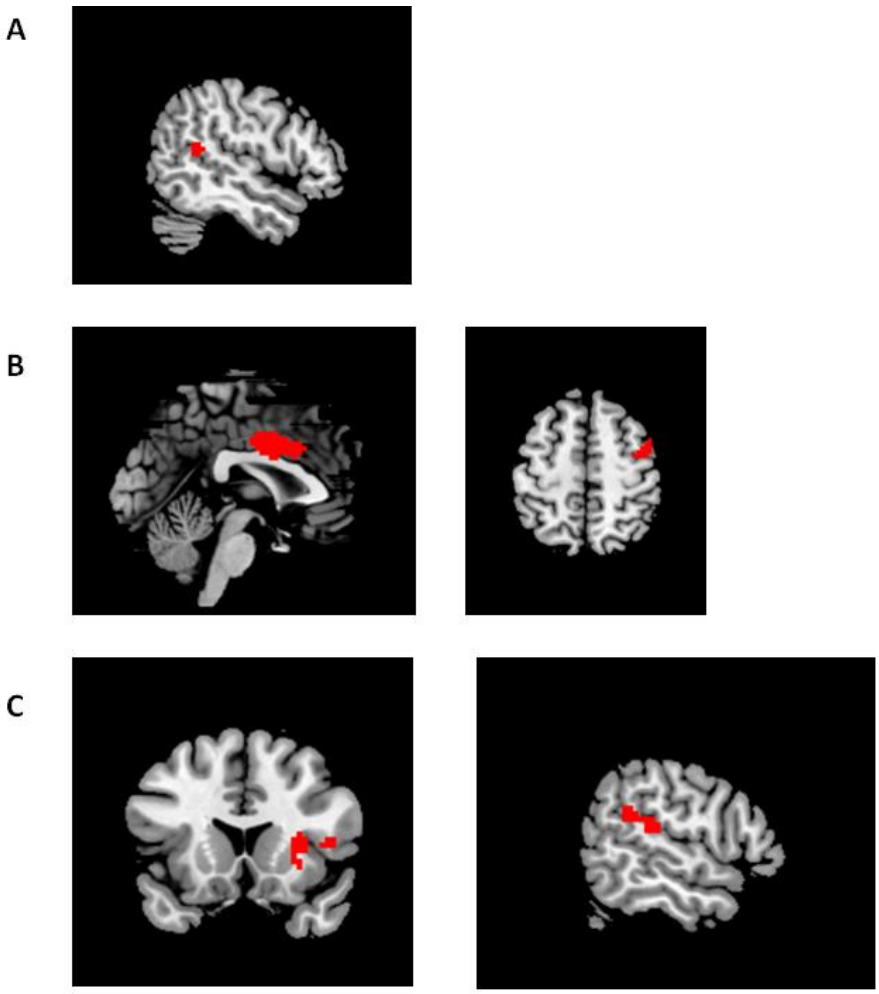


Figure 1: Results of the fMRI analysis. A) Sagittal view of the right STS (51, -45, 15), active during the action phase for the main effect of imitation. B) Axial view of the IFG (57, 12, 33) and coronal view of the aMCC (0, 18, 33), active during the pain perception phase for the main effect of pain. C). Coronal view of the right dorsal AI (30, 15, 6) and sagittal view of the right TPJ (57, -42, 24), active during the pain perception phase for the interaction effect between pain and imitation.

In the pain perception phase, we specifically expected to observe activity in areas of the so-called pain matrix (ACC and AI). For the main effect of pain, peak activity was found the anterior medial cingulate cortex (aMCC; 0, 18, 33, z = 4.21) and in the bilateral inferior frontal gyrus (IFG; 57, 12, 33, z = 6.18 and -57, 9, 36, z = 6.78; see Figure 1B). Although the focus of this activation was not in the AI, activity was found in the right ventral AI (43, 29, 7) and bilateral mid insula (42, 0, 16 and -38, 0, 14). For the interaction effect, activation was found in the right dorsal AI (30, 15, 6, z = 5.69) and the right TPJ (57, -42, 24, z = 5.29; see Figure 1C). Paired *T*-tests clearly showed that this activity was due to an increase of percentage signal change in the PainImitation condition compared to the PainNonimitation condition, $t(17) = 3.92$, $p = .001$ and $t(17) = 4.25$, $p = .001$ for the right dorsal AI (see Figure 2A) and the right TPJ (see Figure 2B) respectively, while no difference was found between the neutral conditions, $t(17) = -.14$, $p > .88$ and $t(17) = .73$, $p > .47$. Interestingly, in the PainImitation condition only, a positive correlation was observed between percentage signal change in the right dorsal AI and right TPJ, $r = .75$, $p = .001$ (after removal of one outlier according to Cook's distance; see Figure 3).

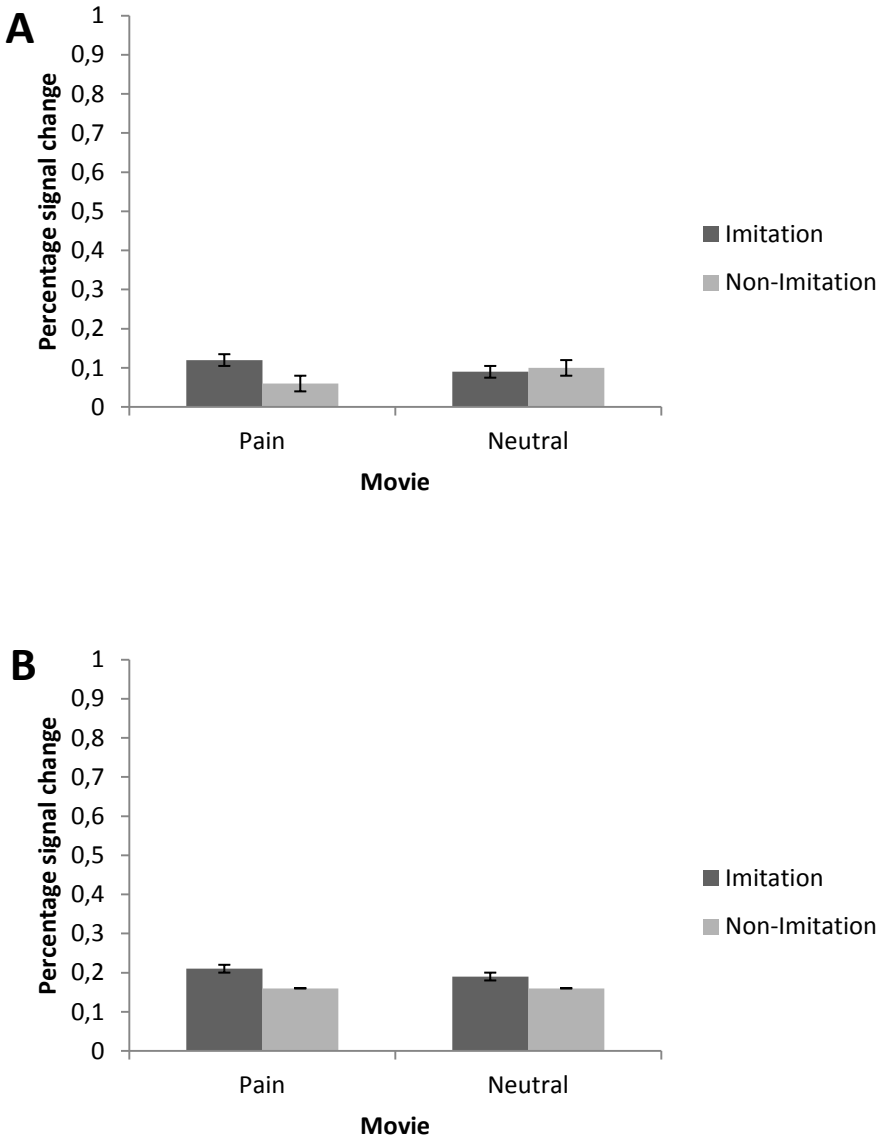


Figure 2: Percentage signal change analysis for the areas obtained in the interaction analysis during the pain perception phase. A) Right dorsal AI (30, 15, 6). B) Right TPJ (57, -42, 24).

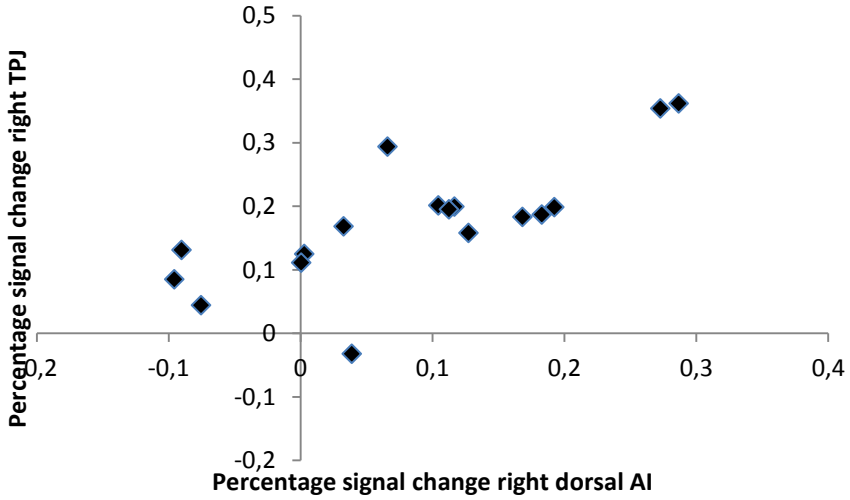


Figure 3: Correlation between percentage signal change in the right dorsal AI and right TPJ in the PainImitation condition.

Additionally, we conducted a percentage signal change analysis for areas highlighted in Lamm et al. (2011), where it was found that both for the region containing the putamen and AI (extending to inferior frontal gyrus; 24, 18, 6, z = 4.77; see Figure 4A) and the dorsal AI (39, 12, 15, z = 4.20; see Figure 4B) significant differences was observed for the contrast between PainImitation and PainNonimitation, $t(17) = 3.56$, $p < .01$ and $t(17) = 2.42$, $p < .05$ respectively.

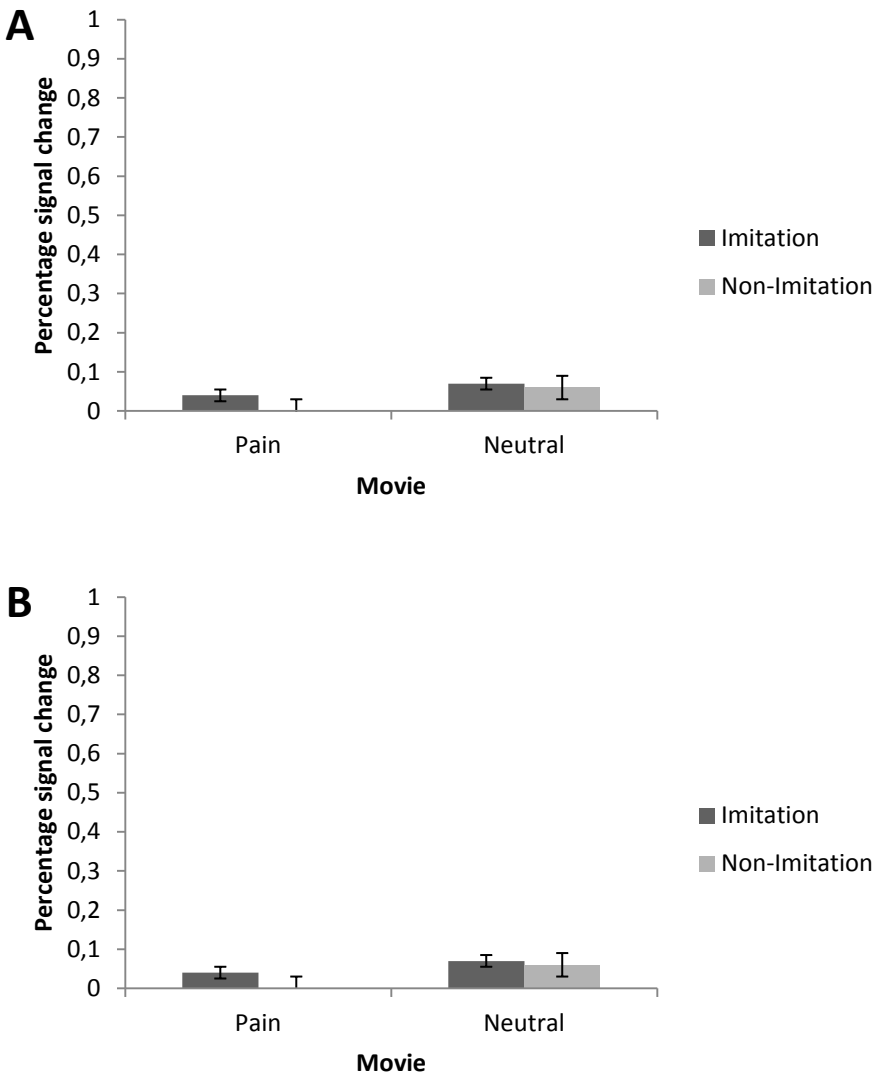


Figure 4: Percentage signal change analysis for areas obtained via Lamm et al. (2011). B) The putamen and AI (extending to inferior frontal gyrus; 24, 18, 6). C) The dorsal AI (39, 12, 15).

DISCUSSION

The current fMRI study directly investigated the influence of being imitated on empathy for pain. The experiment consisted of an action phase where participants were being imitated or not by a hand on screen and a pain perception phase where this hand received a painful or non-painful stimulation. First, it was observed that during the action phase, being imitated compared to not being imitated elicited activation in the right posterior STS. During the pain perception phase, a main effect of pain was found in the aMCC, confirming previous findings (e.g. Lamm et al., 2011; Singer et al., 2004). Finally, the interaction during the pain perception phase showed an effect in the right dorsal AI and right TPJ. Percentage signal analyses confirmed that this effect was driven by higher activity when observing pain after being imitated.

During the action phase, stronger activity was found in the right posterior STS when being imitated compared to not being imitated. This region has been shown to be important in action observation (see Grèzes & Decety, 2001 for a meta-analysis) and imitation (Iacoboni et al., 2001; Molenberghs, Brander, Mattingley, & Cunnington, 2010), Interestingly, a study on reciprocal imitation by Decety, Chaminade, Grèzes, & Meltzoff (2002) found activation in the posterior STS not only for imitation but also for being imitated. This region has been thought to be related to the mirror neuron system (MNS), providing visual representations of observed actions that are then transferred to classical mirror areas (Tessari, Canessa, Ukmar, Rumiati, 2007). Furthermore, it has been argued that the posterior STS is involved in monitoring the congruency between observed and executed actions (Miall et al., 2006; Molenberghs et al., 2010). Finally, the posterior STS has been strongly linked to perception of biological motion stimuli (e.g.

Grossman, Battelli, & Pascual-Leone, 2005; van Kemenade, Muggleton, Walsh, & Saygin, 2012). Most likely, the stronger activation in the posterior STS when being imitated reflects increased attention to the movement of another person when these movements match our own.

Importantly, the main effect of pain showed activation in the IFG and aMCC, replicating previous research (see Lamm et al., 2011 for a meta-analysis). Theories suggest that the aMCC plays an important role in homeostatic regulation and preparing appropriate responses to painful and aversive event (Morrison and Downing, 2007). Activation of the inferior frontal cortex has been related to action observation (Van Overwalle and Baetens, 2009) as a reflection of action understanding (Rizzolatti, Ferrari, Rozzi, & Fogassi, 2006). Interestingly, our main effect showed no peak activation in the AI, although activation of the inferior frontal gyrus seemed to be extending to the ventral part of the AI. As suggested by Lamm and Singer (2010), ventral and dorsal parts of the AI might serve different functions. While the ventral part might play a dominant role in the processing of core affective states, the dorsal AI might be more related to motor control and homeostatic regulation. This would be in line with the current results, suggesting that the main effect of pain activates the ventral AI important for affective sharing without strong modulation of self-relevance. Furthermore, Lamm and Singer (2010) suggest that this part of the AI shows strong connections to the amygdala, an area also shown to be active in the current experiment. Finally, the main effect of pain showed activity in the bilateral mid insula. This part of the insula has been related to sensory discrimination, reflecting changes in sensory intensity (Craig, Chen, Bandy, & Reiman, 2000; Critchley, Wiens, Rotshtein, Öhman, & Dolan, 2004; Lin, Hsieh, Yeh, Lee, & Niddam, 2013). Again, this region was not

modulated by being imitated, suggesting that this manipulation did not affect subdivision of the insula related to sensory processing.

Most importantly, when looking at areas specifically activated when observing pain after being imitated, the right dorsal part of the AI and the right TPJ were found. As mentioned above, the dorsal AI has been related to viscero-motor functions, adapting behaviour by translating emotional states into action tendencies. This is in line with results shown by De Coster et al. (2014) that being imitated elicits a facilitation of motor evoked potentials when observing pain, indicating preparation for withdrawal action tendencies. Moreover, since we expected being imitated to increase self-other overlap, we predicted to find activity in the right TPJ, a structure related to self-other distinction (Brass et al., 2001; Brass et al., 2009; Spengler et al., 2010). A meta-analysis of Sperduti, Delaveau, Fossati, and Nadel (2011) links TPJ to externally triggered agency. They suggest that activity in this area represents a general mismatch detection mechanism. Decety and Lamm (2007) also suggest that the TPJ serves to compare internal predictions with external events. The current findings suggest that observing pain after being imitated produces greater mismatch between internal (self) and external (other) representations. At first sight, it is surprising that we found stronger TPJ activity in the being imitated condition where the match between the observed and executed movement is high given that previous studies found stronger activation in incongruent compared to congruent conditions (Brass et al., 2009). However, it is important to note that TPJ activation in the current study was found in the pain perception phase rather than the action phase. Furthermore, the activation showed up in the interaction contrast of (PainImitation – PainNonimitation) – (NeutralImitation – NeutralNonimitation), cancelling out motor influences. Thus, one reasonable interpretation might be that the right TPJ was involved

in distancing oneself from the observed pain (after being imitated) specifically. This interpretation would be in line with the strong positive correlation found between percentage signal change in the right dorsal AI and right TPJ, suggesting that higher AI activation was associated with a stronger need for distancing.

In sum, the current study shows that being imitated increases reactions to observing someone else in pain. Activation in the right dorsal AI suggested stronger affective responding after being imitated, while activity in the right TPJ indicated a stronger need to distinguish self from other when observing someone else in pain. The current results provide a first direct link between literature on being imitated and empathy for pain, and support the idea that self-other overlap is an important process that combines both.

REFERENCES

Brass, M., Ruby, P., & Spengler, S. (2009). Inhibition of imitative behaviour and social cognition. *Philosophical Transactions of the Royal Society B-Biological Sciences, 364*, 2359-2367. doi: 10.1098/rstb.2009.0066

Brass, M., Zysset, S., & von Cramon, D. Y. (2001). The inhibition of imitative response tendencies. *Neuroimage, 14*, 1416-1423. doi: 10.1006/nimg.2001.0944

Chartrand, T. L., & Bargh, J. A. (1999). The Chameleon effect: The perception-behaviour link and social interaction. *Journal of Personality and Social Psychology, 76*, 893-910. doi: 10.1037/0022-3514.76.6.893

Cheng, Y., Lin, C-P., Liu, H-L., Hsu, Y-Y., Lim, K-E., Hung, D., & Decety, J. (2007). Expertise modulates the perception of pain in others. *Current Biology, 17*, 1708-1713. doi: 10.1016/j.cub.2007/09/020

Craig, A. D., Chen, K., Bandy, D., & Reiman, E. M. (2000). Thermosensory activation of insular cortex. *Nature Neuroscience, 3*, 184-190. doi: 10.1038/72131

Critchley, A. D., Wiens, S., Rotshtein, P., Öhman, A., & Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nature Neuroscience, 7*, 189-195. doi: 10.1038/nn176

Decety, J., Chaminade, T., Grèzes, J., & Meltzoff, A. N. (2002). A PET exploration of the neural mechanisms involved in reciprocal imitation. *Neuroimage, 15*, 265-272. doi: 10.1006/nimg.2001.0938

Decety, J., Echols, S. C., & Correll, J. (2009). The blame game: the effect of responsibility and social stigma on empathy for pain. *Journal of Cognitive Neuroscience, 22*, 985-997. doi: 10.1162/jocn.2009.21266

Decety, J., & Lamm, C. (2006). Human empathy through the lens of social neuroscience. *The Scientific World Journal, 6*, 1146-1163. doi: 10.1100/tsw.2006.221

Decety, J., & Lamm, C. (2007). The role of the right temporoparietal junction in social interaction: how low-level computational processes contribute to meta-cognition. *Neuroscientist, 13*, 580-593. doi: 10.1177/1073858407304654

De Coster, L., Andres, M., & Brass, M. (2014). Effects of being imitated on motor responses evoked by pain observation: exerting control determines action tendencies when perceiving pain in others. *The Journal of Neuroscience, 34*, 6952-6957. doi: 10.1523/JNEUROSCI.5044-13.2014

De Coster, L., Verschuere, B., Goubert, L., Tsakiris, M., & Brass, M. (2013). I suffer more from your pain when you act like me: Being imitated enhances affective responses to seeing someone else in pain. *Cognitive, Affective, & Behavioral Neuroscience, 13*, 519-532. doi: 10.3758/s13415-013-0168-4

de Vignemont, F., & Singer, T. (2006). The emapthic brain: How, when, and why? *Trends in Cognitive Sciences, 10*, 435-441. doi: 10.1016/j.tics.2006.08.008

Goubert, L., Vervoort, T., & Craig, K. D. (2012). Empathy and pain. In R. F. Schmidt & G. F. Gebhart (Eds.), *Encyclopedia of Pain, Second Edition.* Heidelberg: Springer-Verlag.

Grèzes, J., & Decety, J. (2001). Functional anatomy of execution, mental simulation, observation, and verb generation of actions: a meta-analysis. *Human Brain Mapping, 12*, 1-19. doi: 10.1002/1097-0193(200101)12

Grossman, E. D., Battelli, L., & Pascual-Leone, A. (2005). Repetitive TMS over posterior STS disrupts perception of biological motion. *Vision Research, 45*, 2847-2853. doi: 10.1016/j.visres.2005.05.027

Han, S. H., Fan, Y., & Mao, L. (2008). Gender difference in empathy for pain: an electrophysiological investigation. *Brain Research, 1196*, 85-93. doi: 10.1016/jbrainres.2007.12.062

Hein, G., & Singer, T. (2008). I feel how you feel but not always: The empathic brain and its modulation. *Current Opinion in Neurobiology, 18*, 153-158. doi: 10.1016/j.conb.2008.07.012

Iacoboni, M., Koski, L. M., Brass, M., Bekkering, H., Woods, R. P., Dubeau, M. C., Mazziotta, J. C., Rizzolatti, G. (2001). Reafferent copies of imitated actions in the right superior temporal cortex. *Proceedings of the National Academy of Sciences of the United States of America, 98*, 13995-13999. doi: 10.1073/pnas.241474598

Jackson, P. L., Meltzoff, A. N., & Decety, J. (2005). How do we perceive the pain of others?A window into the neural processes involved in empathy. *Neuroimage, 24*, 771-779. doi: 10.1016/j.neuroimage.2004.09.006

Keysers, C., Kaas, J. H., & Gazzola, V. (2010). Somatosensation in social perception. *Nature Reviews Neuroscience, 11*, 417-428. doi: 10.1038/nrn2833

Kühn, S., Muller, B. C., van Baaren, R. B., Wietzker, A., Dijksterhuis, A., & Brass, M. (2010). Why do I like you when you behave like me? Neural mechanisms mediating positive consequences of observing someone being imitated. *Social Neuroscience, 5,* 384-392. doi: 10.1080/17470911003633750

Lakin, J. L., Chartrand, T. L., & Arkin, R. M. (2008). I am too just like you – Nonconscious mimicry as an automatic behavioral response to social exclusion. *Psychological Science, 19,* 816-822. doi: 10.1111/j.1467-9280.2008.02162.x

Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage, 54,* 2492- 2502. doi: 10.1016/j.neuroimage.2010.10.014

Lamm, C., Meltzoff, A. N., & Decety, J. (2010). How do we empathize with someone who is not like us? A functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience, 22,* 362-376. doi: 10.1162/jocn.2009.21186

Lamm, C., & Singer, T. (2010). The role of the anterior cingulate cortex in social emotions. *Brain Structure & Function, 214,* 579-591. doi: 10.1007/s00429-010-0251-3

Lin, C.-S., Hsieh, J.-C., Yeh, T.-C., Lee, S.-Y., & Niddam, D. M. (2013). Functional dissociation within insular cortex: The effect of pre-stimulus anxiety on pain. *Brain Research, 1493,* 40-47. doi: 10.1016/j.brainres.2012.11.035

Miall, R.C., Stanley, J., Todhunter, S., Levick, C., Lindo, S., & Miall, J. D. (2006). Performing hand actions assists the visual discrimination of similar hand postures. *Neuropsychologia, 44,* 966-976. doi: 10.1016/j.neuropsychologia.2005.09.006

Molenberghs, P., Brander, C., Mattingley, J. B., Cunnington, R. (2010). The role of the superior temporal sulcus and the mirror neuron system in imitation. *Human Brain Mapping, 31,* 1316-11326. doi: 10.1002/hbm.20938

Morrison, I., & Downing, P. E. (2007). Organization of felt and seen pain responses in anterior cingulate cortex. *Neuroimage, 37,* 642-651. doi: 10.1016/j.neuroimage.2007.03.079

Oldfield, R. C. (1971). The assessment and analysis of handedness. *Neuropsychologia, 9,* 97- 113.

Rizzolatti, G., Ferrari, P. F., Rozzi, S., & Fogassi, L. (2006). The inferior parietal lobule: where action becomes perception. *Novartis Foundation Symposium, 270,* 129-140 (discussion 140-125, 164-129).

Singer, T., Seymour, B., O' Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for Pain Involves the Affective but not Sensory Components of Pain. *Science, 303,* 1157-1162. doi: 10.1126/science.1093535

Singer, T., Seymour, B., O' Doherty, J. P., Stephan, K. E., Dolan, R. J., & Frith, C. D. (2006). Empathic neural responses are modulated by the perceived fairness of others. *Nature, 439,* 466-469. doi: 10.1038/nature04271

Spengler, S., von Cramon, D. Y., & Brass, M. (2010). Resisting motor mimicry: Control of imitation involves processes central to social cognition in patients with frontal and temporo-parietal lesion. *Social Neuroscience, 19,* 98-106. doi: 10.1080/17470911003687905

Sperduti, M., Delaveau, P., Fossati, P., & Nadel, J. (2011). Different brain structures related to self- and external-agency attribution: a brief review and meta-analysis. *Brain Structure and Function, 216,* 151-157. doi: 10.1007/s00429-010-0298-1

Stel, M., van Baaren, R. B., & Vonk, R. (2008). Effects of mimicking: Acting prosocially by being emotionally moved. *European Journal of Social Psychology, 38,* 965-976. doi: 10.1002/ejsp.472

Tessari, A., Canessa, N., Ukmar, M., & Rumiati, R. I. (2007). Neuropsychological evidence for a strategic control of multiple routes in imitation. *Brain, 130,* 1111-1126. doi: 10.1093/brain/awm003

van Kemenade, B. M., Muggleton, N., Walsh, V., & Saygin, A. P. (2012). Effects of TMS over premotor and superior temporal cortices on biological motion perception. *Journal of Cognitive Neuroscience, 24,* 896-904. doi: 10.1162/jocn_a_00194

Van Overwalle, F., & Baetens, K. (2009). Understanding others' actions and goals by mirror and mentalizing systems: a meta-analysis. *Neuroimage, 48,* 564-584. doi: 10.1016/j.neuroimage.2009.06.009

Yang, C. Y., Decety, J., Lee, S. Y., Chen, C. Y., & Cheng, Y. W. (2009). Gender differences in the mu rhythm during empathy for pain: An electroencephalographic study. *Brain Research, 1252,* 176-184. doi: 10.1016/j.brainres.2008.11.062

Xu, X. J., Zuo, X. Y., Wang, X. Y., & Han, S. H. (2009). Do you feel my pain? Racial group membership modulates empathic neural responses. *Journal of Neuroscience, 29,* 8525-8529. doi: 10.1523/JNEUROSC.2418-09.2009

CHAPTER 5
THE INFLUENCE OF BEING IMITATED ON EMPATHY FOR PAIN IN ADULTS WITH HIGH FUNCTIONING AUTISM[1]

Imitation and empathy skills are thought to be impaired in adults with high functioning autism (HFA), and have theoretically been linked to dysfunctional shared representational mechanisms. However, research on imitation and empathy deficits show conflicting results. In a previous study, we have related imitation literature and research on observing others in pain in typically developing (TD) adults. It was shown that being imitated enhances affective responding to seeing someone else in pain, and we provided evidence for the role of shared representations as a core underlying mechanism. Behavioural and physiological results in this new study showed that overall affective responses while watching pain movies were the same, if not higher, in adults with HFA compared to TD. Furthermore, TD showed higher affective responding after being imitated during the whole experiment, replicating previous studies. Adults with HFA, however, showed a reversal of the effect over time: while affective responding was lower after being imitated during the first half of the experiment, affective responding in the second half of the experiment was higher after being imitated. These results suggest dysfunctional control over these shared representational systems in adults with HFA.

[1] De Coster, L., Wiersmea, R., Deschrijver, E., & Brass, M. (in preparation). The influence of being imitated on empathy for pain in adults with high functioning autism.

INTRODUCTION

Autism spectrum disorder (ASD) is a pervasive neurodevelopmental disorder characterized by abnormalities in social communication and interaction and restricted and repetitive patterns of behaviour, interests, or activities (DSM-5, American Psychiatric Association, 2013). Thus, individuals with ASD often experience difficulties with daily interactions and communications, such as interpreting body language, reading facial expressions, and understanding others' thoughts and desires (e.g. Centelles, Assaiante, Etchegoyhen, Bouvard, & Schmitz, 2013; Poljac, Poljac, & Wagemans, 2013; Senju, 2012). A prominent theory of ASD deficits in social cognition is the so-called 'broken mirror' hypothesis. This hypothesis suggests that deficits in social cognition are the result of a dysfunctional mirror neuron system (MNS; Williams, Whiten, & Singh, 2004). This hypothesis is based on the idea that we can understand other people's actions and emotions by embodied simulation of their motor and emotional states (e.g. Bastiaansen, Thioux, & Keysers, 2009; Brass & Heyes, 2005; Brass, Ruby, & Spengler, 2009; Gazzola, Aziz-Zadeh, & Keysers, 2006; Kaplan & Iacoboni, 2006; Rizzolatti & Craighero, 2004; Rizzolatti & Sinigaglia, 2010). According to this hypothesis, ASD should be related to two core social-cognitive deficits, namely imitation and empathy.

The nature of these abnormalities, however, is still a matter of debate, with various contradicting findings dominating the literature. Regarding imitation deficits in ASD, early research suggest reduced imitation (for a review see Williams et al., 2004). However, other studies have observed no imitation deficit (Avikainen, Kulomaki, & Hari, 1999; Bird, Leighton, Press, & Heyes, 2007; Dinstein et al., 2010; Ruysschaert, Warreyn, Wiersema,

Oostra, & Roeyers, 2014) or even an opposite pattern in ASD, namely hyperimitation (Spengler, Bird, & Brass, 2010). Furthermore, several clinical features such as echolalia (unintentionally repeating others' speech) and echopraxia (unintentionally repeating others' actions) seem to be in line with heightened imitation in ASD (Rutter, 1974; Russell, 1997; Williams et al., 2004). Research on the effects of being imitated in ASD, however, has been relatively limited. Studies looking at the effect of being imitated in ASD have reported improved social behaviour (Dawson & Adams, 1984; Escalona, Field, Nadel, & Lundy, 2002; Field, Field, Sanders, & Nadel, 2001). Furthermore, it was suggested that imitation is beneficial to children with ASD because it creates a feeling of shared understanding between two persons (Dawson & Adams, 1984; Nadel & Peze, 1993). As mentioned above, the MNS has been thought to be important in action understanding and simulation others' emotional and motor states (Bastiaansen et al., 2009; Gazzola et al., 2006; Kaplan & Iacoboni, 2006; Rizzolatti & Craighero, 2004; Rizzolatti & Sinigaglia, 2010). Moreover, it is now widely assumed that the function of mirror neurons is based on motor simulation of an observed action that is mapped onto a corresponding motor representation in the observer (for a review see Brass & Heyes, 2005). While the broken-mirror hypothesis has not made any explicit predictions on deficits in being imitated in ASD, a deficit in MNS would predict problems in motor simulation and thus altered effect of being imitated. Furthermore, Oberman and Ramachandran (2007) postulate that dysfunctional simulation mechanisms in ASD might underlie the wide range of social and communicative deficits seen in these individuals.

Findings on empathy abnormalities in adults with ASD have not been straightforward either. Empathy has been defined as 'the ability to form an embodied representation of another's emotional state, while at the same time

being aware of the causal mechanism that induced the emotional state in the other' (Gonzalez-Liencres, Shamay-Tsoory, & Brune, 2013). It has been argued to be deficient in adults with ASD (Baron-Cohen & Wheelwright, 2004). While early research suggested an absence of embodied empathy and reduced emotional resonance in adults with ASD (e.g. Minio-Paluello, Baron-Cohen, Avenanti, Walsh, & Aglioti, 2009), more recent research suggests intact emotional responses to painful observation (e.g. Hadjikhani et al., 2014). Furthermore, several studies indicate a distinction between abnormalities in cognitive compared to emotional empathy in adults with ASD. Cognitive empathy, defined as emotion understanding requiring perspective taking and mentalizing, has been closely linked to Theory of Mind (ToM). Impairments in ASD concerning ToM and mentalizing have been widely reported (see Senju, 2012 for a review). However, emotional empathy, consistent of emotional contagion (forming of a representation of the other person's feelings, and thereby sharing of the experience; Gallese & Sinigaglia, 2011) and emotional arousal, has been shown to be preserved, if not increased in ASD (Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007; Smith, 2006; Smith, 2009).

The aim of the present study is to further investigate whether people with ASD have problems in being imitated and empathy. In a recent study, De Coster and colleagues (2013) developed a paradigm that showed that being imitated increases affective responses to seeing someone else in pain, due to increased self-other confusion. In this setup, participants are being imitated by a videotaped hand or not (appearing on screen), and the hand on screen subsequently receives painful stimulation. Using self-report and physiological measures such as startle blink reflex and skin conductance, it was observed that being imitated by the hand on screen leads to higher reactions to observing that hand in pain. Furthermore, it was shown that the

influence of being imitated on empathy for pain was mediated by an increase in self-other overlap. In the current study, we used this paradigm to test whether these effects are also observed in adults with high functioning autism (HFA). This paradigm allows investigating imitation and empathy at the same time. First, theoretical accounts that assume that empathy is impaired in ASD predict that these individuals should show reduced empathy for pain. Furthermore, theories suggesting that adults with ASD show hypo-activity in the MNS should predict that being imitated should have a reduced influence on empathy for pain since motor simulation and self-other merging should be impaired.

MATERIALS AND METHODS

Participants

Twenty adults with HFA and 20 TD controls, aged 21 – 48 years and all right-handed, participated in the study in exchange for 20 Euros. Adults with HFA (10 F, 10 M) were recruited via the Flemish Autism Association, while TD adults (10 F, 10 M) were recruited via the university pool of subjects. Adults with HFA were required to have an official clinical diagnosis of ASD by a multidisciplinary team. Furthermore, their status as 'high-functioning' was derived from their performance on a standardized cognitive assessment using the Kaufman 2 short form of the WAIS-III ($IQ \geq 80$; see below; Minshew, Turner, & Goldstein, 2005). Both groups did not have any additional neurological disorders. The study was granted ethical approval by the local ethics committee, and all participants provided written consent beforehand. Adults with HFA scored significantly higher than TD adults on the Autism Quotient (AQ; Baron-Cohen, Wheelwright, Skinner,

Martin, & Clubley, 2001). Furthermore, all adults with HFA scored above the Social Responsiveness Scale for Adults (SRS-A; Constantino et al., 2003; Bölte, Westerwald, Holtmann, Freitag, & Poustka, 2011) clinical threshold, while no TD adults met this criterion.

Experimental design

Blocks of trials consisted of two phases: an action phase in which movements of the subjects were imitated (imitation block) or not (non-imitation block), and a pain perception phase which immediately followed the action phase. In the pain perception phase, one of nine pain movies was presented (*'bore goes into the hand'*, *'hammer is smacked on the hand'*, *'hot iron is pressed on the hand'*, *'nail is knocked into the hand with a hammer'*, *'nail of the ring finger is pulled out of the hand'*, *'paper makes a paper cut in the hand'*, *'pinchers pinch the hand'*, *'sandpaper is rubbed over the hand'*, *'stapler puts a staple into the hand'*). Each pain movie was combined two times with both an imitation and non-imitation block, presenting a startle probe during the pain movies to elicit the startle blink reflex once after each type of block. This resulted in a total of 36 trials: each of the nine pain movies was thus combined with both imitative (imitation and non-imitation) and both startle (startle and no startle) conditions. The association of the different pain movies with the different block and startle conditions was completely randomized across participants.

Stimuli and apparatus

Stimulus material consisted of three types of 720 x 576 video-clips created by professionals: a hand in a resting position, simple finger movements (for the action phase of the task), and pain movies showing a hand receiving pain stimulation (for the pain movies in the pain perception phase).

In the resting state video clip, a right hand with palm down and fingers slightly spread was shown, matching the position of the right hand of participants placed on the response box. This video remained on screen in between presentation of the other videos in order to assure continuous observation of a right hand on screen.

During the action phase of the experimental task, participants carried out simple finger movements of the index, middle, ring, or little finger. These finger movements were recorded with a custom-built response device using light sensors. This device allowed us to use finger lifting movements of participants as triggers for the presentation of the appropriate finger movement video. Temporal resolution was optimized (see Procedure) so that participants immediately viewed a video-taped finger movement on screen after initiating a finger movement with their own hand. For example, in an imitation block, the lifting of an index finger resulted in the presentation of the index finger lifting video, while the middle, ring, or little finger lifting video was shown in a non-imitation block. All finger movement clips had a total duration of 2000 ms.

The perception phase of the experimental task consisted of the presentation of one of nine pain movies in which painful stimulation was applied to the hand on screen. All movies had a total duration of 8000 ms.

Subjective reports

During the experiment, four behavioural questions were presented after each pain movie, to measure explicit reactions to observing the hand in pain: *'How unpleasant do you think the other person found the pain stimulation?', 'How intense do you think the other person experienced painful sensations?', 'How unpleasant did you find the pain stimulation yourself?', 'How intense did you experience painful sensations yourself?'.* The first two questions refer to painful experiences of the other person, while

the last two questions refer to first person experiences. Both affective (unpleasantness) and sensory (intensity) dimensions of pain had to be rated on a scale from -5 (*not unpleasant/intense at all*) to +5 (*very unpleasant/intense*), since research suggests that both dimensions might be activated when observing someone else in pain (Bufalari et al., 2007; Cheng, Yang, Lin, Lee, & Decety, 2008; Lamm, Nusbaum, Meltzoff, & Decety, 2007; Loggia, Mogil, & Bushnell, 2008; Keysers, Kaas, & Gazzola, 2010). Furthermore, a Dutch translation of the scale of Batson, Fultz, and Schoenrade (1987) was used, presenting seven items measuring two types of emotional responses. These items questioned the subjective feelings of participants while viewing painful stimulation, with four items referring to self-oriented feelings (personal distress; *'While viewing the painful stimulation of the other person I felt worried/distressed/anxious/sad'*), and three items referring to other-oriented feelings (concern; *'While viewing the painful stimulation of the other person I felt understanding/empathetic/compassionate'*). As such, questions referring to the observed painful situations could be divided into two categories: self (Cronbach's α for both groups > .90) versus other (Cronbach's α for both groups > .90).

Procedure

Participants were seated in front of a standard computer screen at arm length, and asked to place the four fingers of their right hand on a custom-made response box. Display of stimulus material and recording of responses were conducted with Presentation software (Neurobehavioral Systems, Inc.). As soon as the video-taped right hand appeared on screen (resting state movie), subjects were instructed to voluntary move a randomly chosen finger that was placed on the response box. Immediately after movement of one of the subjects' fingers (delay = 0 ms, estimate of intrinsic delay of

computer/software = 66.93 ms), a movie was shown in which the hand on screen performed the same or a different movement for imitation and non-imitation blocks respectively. After 20 movements (all imitative or all non-imitative), one of the pain movies was immediately presented. After a pain movie, participants had to rate the 11 behavioural statements on a scale from -5 to +5.

During the pain clips, a burst of white noise of 95 dB(A) was presented after 4000 ms via headphones in only 50 % of the cases in order to avoid predictability of the occurrence of this startle probe (Hawk & Cook, 2000). Prior to the start of the experiment, the startle noise was presented successively five times, in order to control for initial habituation.

Before the start of the experiment, two practice blocks (one of each imitative condition) were presented in order to familiarize subjects with the procedure. The pain movie shown in these practice blocks was not used in the experimental phase. Furthermore, in these practice blocks, it was verified whether participants understood the behavioural questions correctly. More specifically, they were explicitly made aware of the distinction between other- and self-related questions, and of the fact that the question 'How intense did you experience painful sensations yourself?' related to self-experienced painful sensations alone.

At the end of the experiment, the Kaufman 2 short form of the WAIS-III (Minshew et al., 2005) was conducted in order to measure IQ. This short form of the WAIS-III, including the subtests Vocabulary, Similarities, Block Design, and Picture Completion, has been shown to be adequately predictive for total IQ scores. Furthermore, Minshew et al. (2005) have shown that the Kaufman 2 is the most adequate short form for adults with ASD. IQ-scores did not differ significantly between both groups (see Table 1).

Finally, participants were given a set of questionnaires to complete at home (with the possibility of requesting help if necessary). This set included the Interpersonal Reactivity Index (IRI; Davis, 1980) as a measure of dispositional trait empathy, The Fear of Pain Questionnaire-III (FPQ-III; McNeil & Rainwater, 1998) as a measure of fear of experiencing pain in different situations, and the Pain Sensitivity Questionnaire (PSQ; Ruscheweyh, Marziniak, Stumpenhorst, Reinholz, & Knecht, 2009) as a measure of sensitivity for painful stimulation. Furthermore, participants filled in the Adult Self-Report (ASR; Achenbach & Rescorla, 2003) measuring problematic behaviour during the past 6 months, and the Social Responsiveness Scale for adults (SRS-A; Constantino, 2005) to measure social responsiveness and as an index of ASD severity. Table 1 provides an overview with all relevant subtests, details, and *Chi-Square* or *T*-test *p*-values.

Electrophysiological recording and analyses

Psychophysiological signals were registered with a Biopac MP150 System and digitalized using AC1001 – AcqKnowledge Software for Windows with Electronic Manual (Biopac Systems, Inc.).

Startle blink reflex. The startle eye blink reflex was measured according to Blumenthal et al.'s guidelines (2005). Two small Ag/AgCL electrodes (5 mm) were placed over the orbicularis oculi muscle of the left eye, while a ground electrode was placed in the middle of the forehead. The raw EMG signal was amplified with a gain of 5000, filtered with a hardware band pass filter of 0.5 – 500 Hz, and digitally sampled at 1000 Hz, later offline rectified and integrated with PSPHA (De Clercq, Verschuere, De Vlieger, & Crombez, 2006). The magnitude of the eye blink amplitude was computed as the subtraction of the mean rectified baseline value (0 – 20 ms after probe onset) from the rectified peak value in the 21 – 120 ms interval

after probe onset. Trials on which baseline values deviated more than 2.5 *SD* from the mean baseline value of the subject were visually inspected, and if necessary (e.g., movement artefacts, blink onset before probe onset), eliminated. Finally, reflex magnitudes were converted to *T*-scores across trials on a within-participant basis to adjust for between-participant differences in response and baseline EMG magnitude (Funayama, Grillon, Davis, & Phelps, 2001) as follows: *z*-score value = (raw magnitude value – *M* all raw values)/*SD* all raw values; *T*-score value = (*z*-score value x 10) + 50. *Z*-score values were trimmed (all scores below -3 and above +3 were put at -3 and +3 respectively) before they were converted to *T*-scores.

Skin conductance. We measured skin conductance as an index of autonomic functioning that has been shown to be responsive to negative emotional stimuli (Bradley, Codispoti, Cuthbert, & Lang, 2001). Skin conductance was measured using a constant voltage (0.5 V) and two Ag/AgCL electrodes with a diameter of 8 mm. The electrodes were filled with conductive gel and were attached on the thenar and hypothenar eminences of the left hand. Skin conductance was digitized at 10 Hz for the entire duration of the pain movie (8000 ms). Using PSPHA, skin conductance responses were calculated as the difference between the highest and the lowest value in this 8000 ms time window. In order to normalise the data, skin conductance amplitudes were square root transformed prior to analysis (Dawson, Schell, & Fillion, 2000).

Data analysis

A .05 significance level was used in all statistical tests. Due to equipment failure, one participant was excluded from all psychophysiological analyses, and one additional participant was excluded for blink modulation data only (both in the HFA group). The two main

factors of the analysis were Condition (Imitation versus Non-imitation) and Group (HFA versus TD).

Interestingly, a recent study by Cascio, Foss-Feig, Burnette, Heacock, and Cosby (2012) showed a delayed influence of the rubber hand illusion (RHI; Botvinick & Cohen, 1998) in children with ASD, showing a RHI only in the second block of the experiment (after 6 min of stimulation). This illusion, in which a rubber hand feels like one's own hand when being synchronously and simultaneously stroked, comprises of sensory manipulation that is also thought to reflect sharing of representations between self and other (Tajadura-Jiminez, Grehl, & Tsakiris, 2012). Since it was shown that the current paradigm is closely linked to the RHI (De Coster et al., 2013), we decided to evaluate whether the influence of being imitated on empathy for pain might be delayed for adults with HFA compared to TD adults. Furthermore, while conducting the experiment, several adults with HFA indicated to have very different feelings during the beginning compared to the end of the experiment. Therefore, a factor 'Block' was included into the analyses, dividing the experiment in two parts (first versus last 18 trials). A 2 (Condition: Imitation versus Non-imitation) x 2 (Block: 1 versus 2) repeated measure ANOVA was conducted with Group (HFA versus TD) as between subjects factor for all dependent variables.

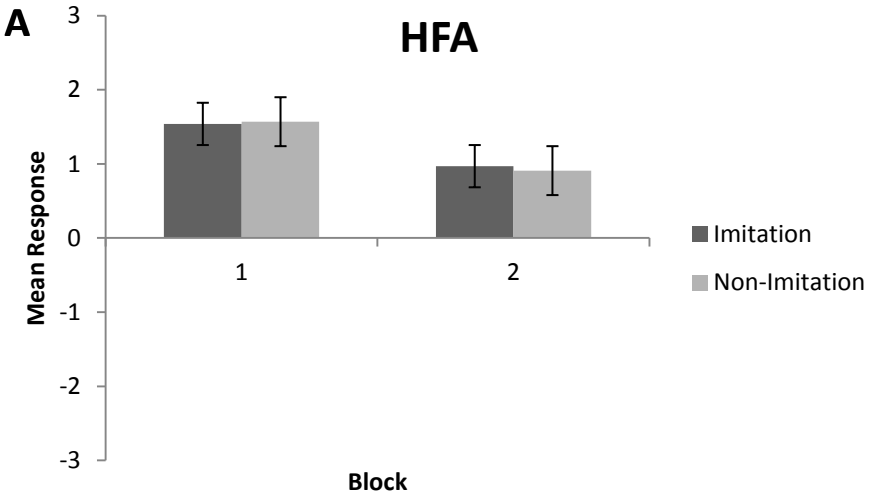
Finally, correlation analyses were performed between questionnaire scores and imitation effects (Imitation – Non-imitation) for both groups separately. However, no significant correlations were found for any of the dependent variables (all *p*s > .05).

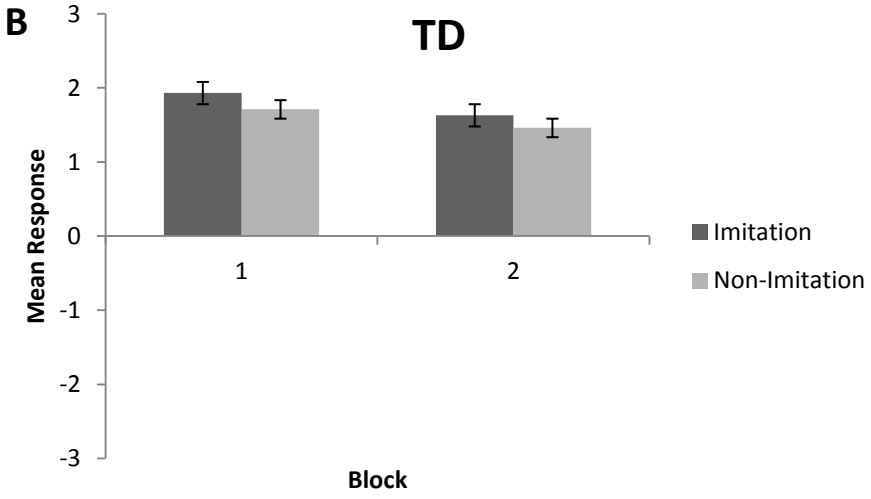
RESULTS

Subjective reports

As mentioned above, all items investigating empathy for pain were divided into other- and self-related questions. Both categories were subsequently analyzed separately. For other-related items, only a main effect of Block, $F(1, 38) = 5.07$, $p < .05$, was observed. Scores were higher in the first ($M = .58$, $SD = 2.41$) compared to the second Block ($M = .21$, $SD = 2.58$) of the experiment. While the interaction with Group was not significant, $F(1, 38) = 1.67$, $p > .20$, Figure 1 suggests that this decline of response scores was mostly present in the HFA group.

Analysis of self-related items revealed a significant main effect of Condition, $F(1, 38) = 5.87$, $p < .05$, indicating higher scores in the Imitation ($M = .46$, $SD = 2.47$) compared to the Non-imitation condition ($M = .34$, $SD = 2.53$). Figure 1 suggests that the imitation effect was more pronounced in the TD group, although the interaction with Group was not significant, $F(1, 38) = 1.04$, $p > .30$. Furthermore, a two-way interaction between Block and Group was observed, $F(1, 38) = 4.84$, $p < .05$. As shown in Figure 1, the effect of Block was only present in the HFA group, $F(1, 19) = 7.33$, $p < .05$, with higher scores in the first ($M = .63$, $SD = 2.62$) compared to the second part ($M = -.07$, $SD = 2.97$) of the experiment. This effect was not significant in the TD group, $F(1, 19) < 1$.


A
HFA
3
2
1
0
-1
-2
-3
Mean Response
1
2
Block
Imitation
Non-Imitation


B
TD
3
2
1
0
-1
-2
-3
Mean Response
1
2
Block
Imitation
Non-Imitation

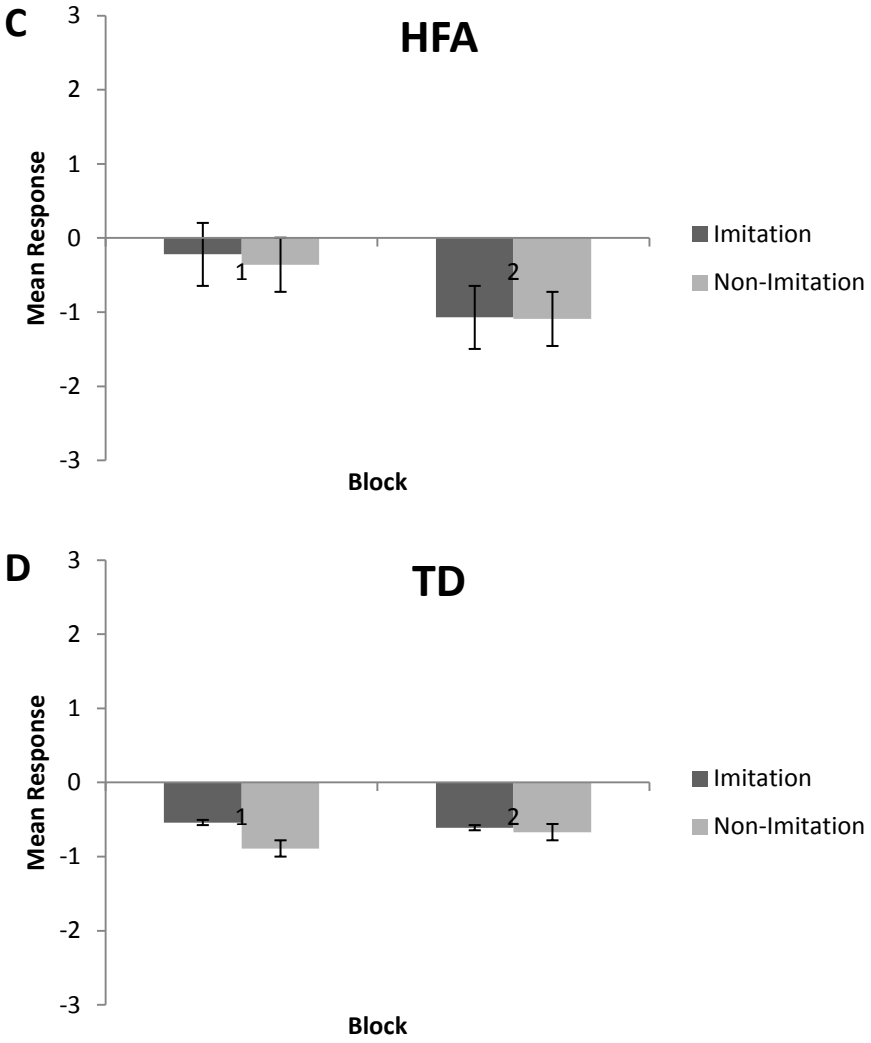


Figure 1: Mean scores (range from -5 to +5) in the imitation and non-imitation condition in the HFA (A, C) and TD group (B, D), for other (A, B)- and self-related (C, D) items referring to pain. Error bars are standard errors of the mean.

Blink modulation

First, no effect of Group was observed, $F(1, 36) = 1.54$, $p > .20$, with scores of adults with HFA ($M = 49.99$, $SD = 2.20$) showing no significant difference from scores of TD adults ($M = 49.28$, $SD = 3.67$). A significant three-way interaction between Group, Condition and Block was found, $F(1, 36) = 4.26$, $p < .05$ (see Figure 3). The two-way interaction between Imitation and Block was significant in the HFA group, $F(1, 17) = 4.83$, $p < .05$, but not in the TD group, $F(1, 19) = 1.47$, $p > .20$. In the TD group, a significant main effect of Condition, $F(1, 19) = 10.07$, $p < .01$, indicated that startle magnitudes were always higher in the Imitation ($M = 51.38$, $SD = 2.97$) compared to the Non-imitation ($M = 46.97$, $SD = 0.74$) condition. However, in the HFA group, startle magnitude was initially lower in the Imitation condition, $t(17) = -2.10$, $p < .05$, while the reverse was numerically, but not statistically, observed in the second Block of the experiment, $t(17) = 1.32$, $p = .21$ (see Figure 2).

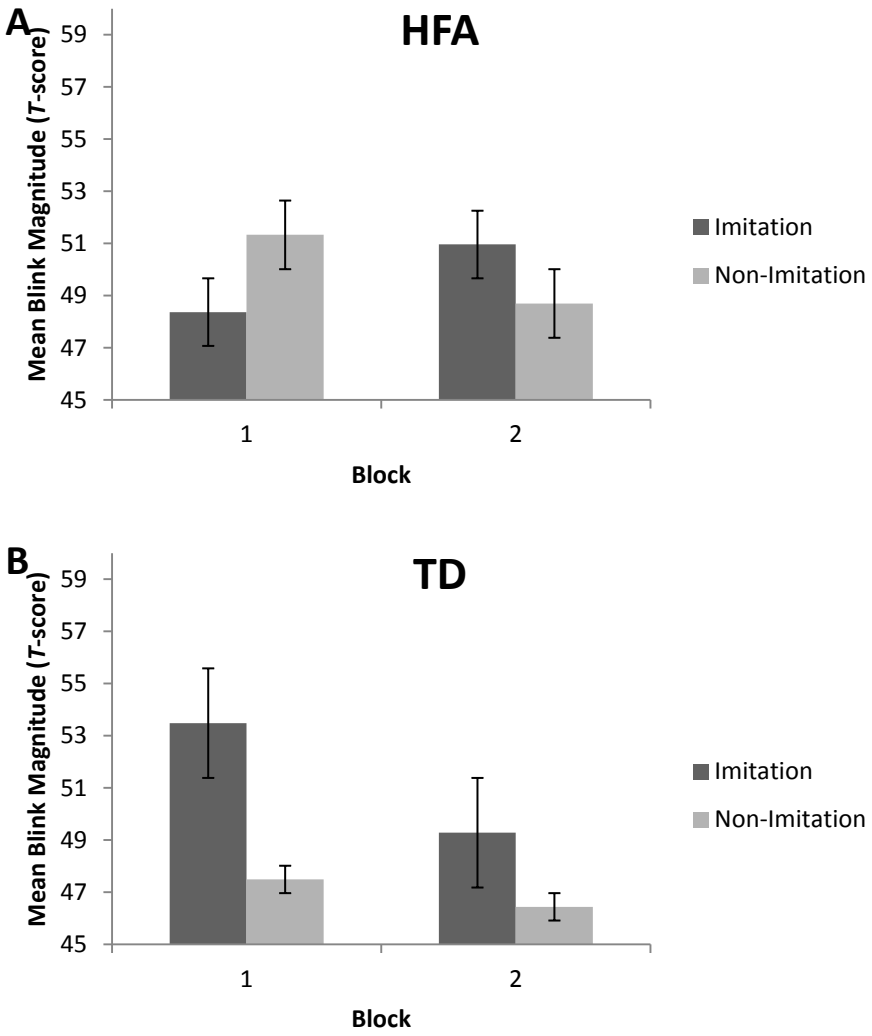


Figure 2: Mean blink magnitude in the imitation and non-imitation condition in the HFA (A) and TD group (B). Magnitude is expressed as within subjects *T*-scores, error bars are standard errors of the mean.

Skin conductance

No effect of Group was observed, $F(1, 37) < 1$; $M = .38$, $SD = .48$ and $M = .27$, $SD = .25$ for adults with HFA and TD adults respectively. However, a significant three-way interaction between Group, Condition and Block was again observed, $F(1, 37) = 5.33$, $p < .05$ (see Figure 3). While the two-way interaction between Imitation and Block was significant in the HFA group, $F(1, 18) = 5.22$, $p < .05$, this was not the case in the TD group, $F(1, 19) < 1$. A significant main effect of Condition, $F(1, 19) = 6.86$, $p < .05$ was again observed in the TD group, indicating higher skin conductance responses in the Imitation ($M = .33$, $SD = .01$) compared to the Non-imitation ($M = .23$, $SD = .00$) condition, irrespective of Block. Although not statistically significant, the typical direction of the effect (higher affective responses after being imitated) was only observed in the second Block of the experiment, $t(18) = 1.58$, $p = .13$, numerically even leading to lower response after being imitated in the first Block of the experiment, $t(18) = -1.38$, $p = .19$ (see Figure 3).

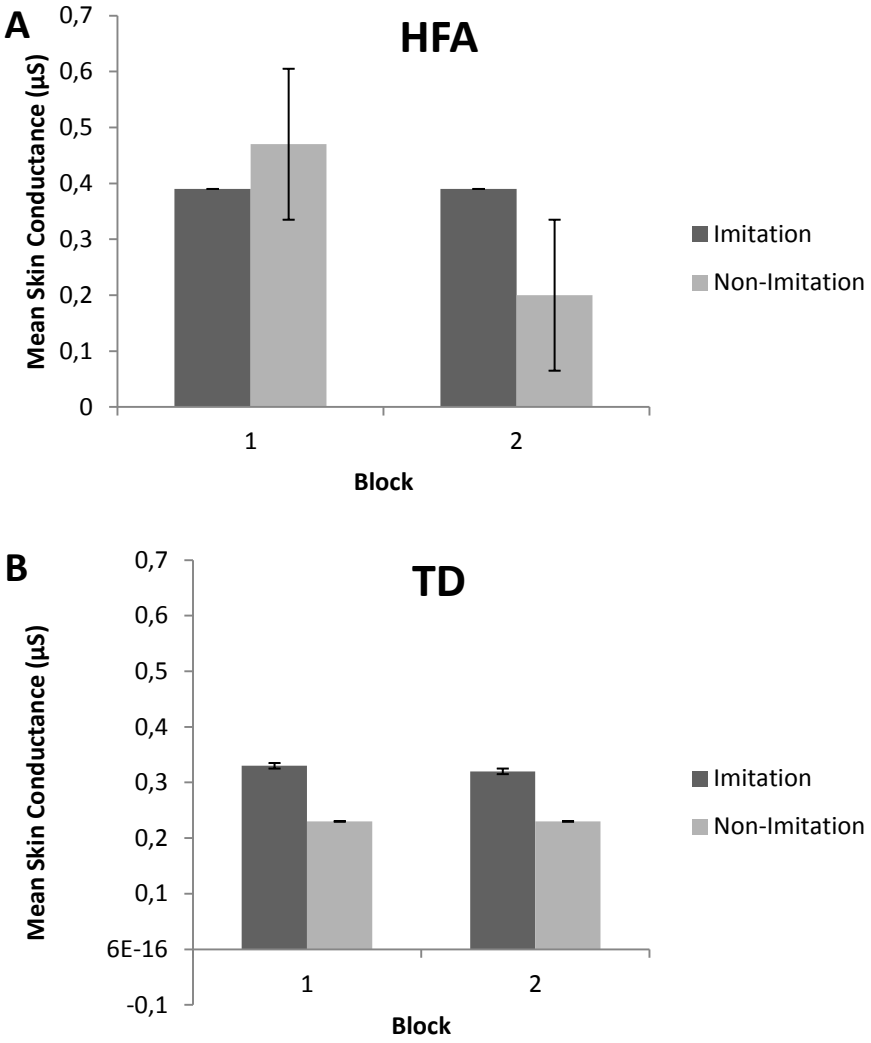


Figure 3: Mean skin conductance in the imitation and non-imitation condition in the HFA (A) and TD group (B). Skin conductance responses are expressed as the difference between the highest and the lowest value in a specified time window, and error bars are standard errors of the mean.

DISCUSSION

Individuals with ASD often show abnormalities in imitation, empathy, and mind-reading abilities. However, the nature and origin of these deficits have been debated extensively. The aim of the current study was to investigate two questions. First, do individuals with ASD show similar empathy for pain than controls? Second, does being imitated have similar social consequences in ASD than in healthy controls? Both questions help to evaluate different hypotheses about the role of the MNS in ASD. One the one hand, it has been argued that ASD is related to impairments in the MNS. If this would hold true, it would suggest that ASD should show less empathy for pain and should be less influenced by being imitated since simulation of emotional and motor states would be deficient. In the current study, we used a recently validated paradigm, in which reactions to observing someone else in pain are heightened after being imitated compared to not being imitated (De Coster et al., 2013). A group of HFA and matched TD adults observed a hand on screen in pain subsequent to being imitated by this hand on screen or not. First, ASD showed similar affective responses to seeing someone else in pain as TD, indicating that no general deficit in empathy for pain was present. Second, while the pattern of TD adults replicated previous findings showing higher empathy for pain after being imitated, adults with HFA showed a distinct pattern of results. Startle blink magnitude and skin conductance, as measures of autonomous nervous functioning, revealed that the influence of being imitated compared to not being imitated on empathy for pain for HFA changed over time. A significant two-way interaction between Block (first and second part of the experiment) and Condition (Imitation versus Non-imitation) showed that affective reactions to observing the hand on screen for adults with HFA were lower after being

imitated in the first part of the experiment, while data in the last part of the experiment mimicked results found for TD adults (higher empathy for pain after being imitated). Furthermore, while subjective reports on self-related items were higher in the imitation compared to the non-imitation condition for both groups, scores decreased significantly for adults with HFA only.

Our study clearly suggests that adults with HFA display empathy for pain when observing someone else in pain. Both for explicit (self-reports) and implicit (startle magnitude, skin conductance) measures, no effect of group was observed, indicating that both ASD and TD showed equal affective responses when observing someone else in pain. This is in line with recent studies showing equal empathic responding in ASD compared to TD (Hadjikhani et al., 2014, Rogers et al., 2007; Smith, 2006; Smith, 2009). Hadjikhani et al. (2014), for example, showed activation of the pain matrix (common areas thought to be active both when experiencing and observing pain, most notably the anterior cingulate cortex and anterior insula; Singer et al., 2004) for a group of subject with ASD and a group of matched control individuals. They concluded that perception-action mechanisms are operant in both ASD and TD, showing that mirror mechanisms and shared representations can be spontaneously elicited in ASD when observing someone else in pain. The current study adds to these findings, showing that being imitated has an influence on empathy for pain in HFA, although the pattern of this influence is different over time for HFA compared to TD. While adults with HFA responded paradoxically to the imitation manipulation in the first block of the experiment, showing reduced influence in the imitation compared to the non-imitation condition, the second block showed a typical influence of being imitated on empathy for pain that was similar to that of TD adults. Thus, the current results suggest a delayed influence of being imitated on empathy for pain, reminiscent of the results of

Cascio et al. (2012), who showed that the RHI in children with ASD was also delayed. These results are in contrast with previously reported lack of empathy and imitation abilities in ASD and the broken mirror theory suggesting that empathic and motor simulation is impossible in ASD due to a deficient MNS (Williams et al., 2004) since this account would predict no empathic response or influence of being imitated. Importantly, our implicit results in the first block of the experiment (statistically for the startle magnitude, numerically for skin conductance) indicate a reversed influence of being imitated on empathy for pain in adults with ASD. This shows that they were sensitive to the imitation manipulation, albeit in an opposite manner. The most plausible interpretation for this finding is that this is due to a compensatory mechanism elicited by reduced control over self-other overlap in ASD.

Recent studies suggest that it is not self-other merging, but rather the control of this merging that is deficient in ASD, linking this process to the temporo-parietal junction (TPJ) and medial prefrontal cortex (mPFC; Spengler et al., 2010; see also Hamilton, 2013). Spengler et al. (2010) suggested that individuals with ASD suffer from heightened rather than decreased self-other merging, resulting in hyperimitation related to social cognitive skills. As shown in a previous study (De Coster et al., 2013), the influence of being imitated on empathy for pain in the current paradigm is mediated by a self-other confusion mechanism. As such, the idea is that ASD show abnormal increase of this self-other merging, especially in the first part of the experiment due to the novelty of the presented stimuli. In this respect, Pellicano and Burr (2012) and van Boxtel and Lu (2013) posit, for example, that people with ASD are overloaded with sensory information accompanying new situations. To cope with this sensation, coping mechanisms might initially make it seem as if being imitated has a reversed

influence on empathy for pain for ASD. Indeed, several subjects reported exactly this strategy when conducting the experiment (e.g. trying to avert attention from stimuli, reminding oneself that the painful sensation was not real). Moreover, ratings on subjective self-reports after observing the hand in pain decreased over the course of the experiment, which might indicate habituation over the time, gradually eliminating the need for coping. Interestingly, recent studies by Paton, Hohwy, and Enticott (2012) and Palmer, Paton, Hohwy, and Enticott (2013) showed that individuals with ASD or individuals scoring high on the nonclinical autism spectrum reported a RHI experience, but discrepancies compared to a control group in sensory and visuotactile-proprioceptive integration were found. These results were also related to different expectancies regarding sensory events in uncertain contexts for ASD, supporting the idea of hypersensitivity in ASD to novel sensory stimuli (such as pain). Thus, research is needed to explore the idea that self-other merging mechanisms change over time in adults with ASD. As mentioned above, studies by Paton et al. (2012) and Palmer et al. (2013) showed differences in the RHI for ASD/nonclinical autism spectrum and control groups. Cascio et al. (2012), however, showed that ASD show a delayed influence of the RHI, suggesting that a sense of body ownership and differentiation of self from other varies over time. Additionally, the role of the TPJ (and MNS) regarding this shift over time should be further investigated. While the study by Hadjikhani et al., (2014) suggests no different activation in these regions between ASD and TD when observing pain, current results suggest that it might be important to look at the time course of these activations. Importantly, research has related ASD to TPJ functioning (Lombardo, Chakrabarti, Bullmore, MRC AIMS Consortium, & Baron-Cohen, 2011). As such, it would be interesting to explore whether

TPJ and/or mPFC activation changes over time in the current experiment for adults with ASD.

Interestingly, literature suggests an important difference between actual and reported empathic sensations in ASD (Bird & Cook, 2013), and a dissociation between emotional/implicit and cognitive/explicit empathy (Smith, 2009). Bird and Cook (2013), for example, suggest that emotional impairments associated with ASD are due to alexithymia – a condition characterized by a reduced ability to identify and describe one's emotional responses, frequently co-occurring with ASD – rather than ASD itself. Furthermore, a study by Fan, Chen, Chen, Decety, & Cheng (2013) has shown that while individuals with ASD show mu suppression and empathic arousal when confronted with other's pain, they display difficulties in responding adequately to other's distress. In light of these discrepancies, part of our subjective explicit results can also be interpreted. Self-related items, measuring self-experienced feelings when observing the hand in pain, showed a general effect of being imitated, without interaction with group or block (although a general decline over blocks was observed for HFA only). This does not correspond to the fact that for physiological measures, people with ASD showed an opposite direction of the imitation effect in early trials, suggesting a discrepancy between explicit and implicit responses in the current study. Taken together, these results might reflect the above mentioned inconsistencies between explicit and implicit empathy (e.g. Smith, 2009). However, previous research suggests that ASD have problems with explicit/cognitive rather than implicit/emotional (Scharzkopf, Schilbach, Vogeley, & Timmermans, 2014; Smith, 2009) measures of empathy. Schwarzkopf et al (2014), for example, have shown that adults with ASD have problems with intentional, explicit perspective taking, while they engage normally in spontaneous perspective taking. This seems in

contrast with the current results where ratings on self-related items were higher after being imitated for both the TD and ASD group. However, as mentioned above, participants in the current study were clearly aware of the difficulties they experienced when confronted with the painful stimulation after being imitated. Thus, it seems plausible that they rated self-related items accordingly and an effect of being imitated was observed, while implicit measures elicited a more unconscious compensatory mechanism. Furthermore, De Coster et al. (2013) have showed that for TD adults, no correlation between explicit and implicit measures was found in the current paradigm, supporting the idea that different processes might modulate explicit and implicit responses differently. Further research is needed, however, to investigate this and examine modulating factors of the imbalance between explicit and implicit forms of empathy in ASD.

Finally, it has to be noted that our skin conductance results seem to suggest that it is the non-imitation condition that changes over the course of the experiment for adults with ASD, and that variability in this condition is large. While this also suggests that the control over self-other merging is deficient in ASD, the difference between being imitated and not being imitated has to be investigated more thoroughly, as well as the discrepancy between both our physiological measures.

REFERENCES

Achenbach, T. M., & Rescorla, L. A. (2003). Manual for the ASEBA Adult Forms & Profiles. Burlington, Vermont: University of Vermont, Research Center for Children, Youth, & Families.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Avikainen, S., Kulomaki, T., & Hari, R. (1999). Normal movement reading in Asperger subjects. *Neuroreport, 10*, 3467-3470. doi: 10.1097/00001758-199911260-00001

Baron-Cohen, S., & Wheelwright, S. (2004). The empathy quotient: an investigation of adults with Asperger syndrome or high functioning, and normal sex differences. *Journal of Autism and Developmental Disorders, 34*, 163-175. doi: 10.1023/B:JADD.0000022607.19833.00

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): evidence from Asperger Syndrome/high-functioning autism, males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders, 31*, 5-17, doi: 10.1023/A:1005653411471

Bastiaansen, J. A. C. J., Thioux, M., & Keysers, C. (2009). Evidence for mirror systems in emotions. *Philophical Transactions of the Royal Society B – Biological Sciences, 364*, 2391-2404. doi: 10.1098/rstb.2009.0058

Batson, C. D., Fultz, J., & Schoenrade, P. A. (1987). Distress and empathy – 2 qualitatively distinct vicarious emotions with different motivational consequences. *Journal of Personality, 55*, 19-39. doi: 10.1111/ 1467-6494.ep8970569

Bird, G., & Cook, R. (2013). Mixed emotions: the contribution of alexithymia to the emotional symptoms of autism. Translational Psychiatry, 3, e285, doi: 10.1038/tp.2013.61

Bird, G., Leighton, J., Press, C., & Heyes, C. (2007). Intact automatic imitation of human and robot actions in autism spectrum disorders. *Proceedings of the Royal Society-B, 274*, 3027-3031. doi: 10.1098/rspb.2007.1019

Bölte, S., Westerwald, E., Holtmann, M., Freitag, C., & Poustka, F. (2011). Autistic traits and autism spectrum disorders: the clinical validity of two measures presuming a continuum of social communication skills. *Journal of Autism and Developmental Disorders, 41*, 66-72. doi: 10.1007/s10803-010-1024-9

Botvinick, M., & Cohen, J. (1998). Rubber hands 'feel' touch that eyes see. *Nature, 391*, 756- 756. doi:10.1038/35784

Bradley, M. M., Codispoti, M., Cuthbert, B. N., & Lang, P. J. (2001). Emotion and motivation I: Defensive and appetitive reactions in picture processing. *Emotion, 1,* 276-298. doi: 10.1037/1528-3542.1.3.276

Brass, M., & Heyes, C. (2005). Imitation: Is cognitive neuroscience solving the correspondence problem? *Trends in Cognitive Sciences, 9*, 489-495. doi: 10.1016/j.tics.2005.08.007

Brass, M., Ruby, P., & Spengler, S. (2009). Inhibition of imitative behaviour and social cognition. *Philosophical Transactions of the Royal Society B-Biological Sciences, 364,* 2359-2367. doi: 10.1098/rstb.2009.0066

Bufalari, I., Aprile, T., Avenanti, A., Di Russo, F., & Aglioti, S. M. (2007). Empathy for pain and touch in the human somatosensory cortex. *Cerebral Cortex, 17*, 2553-2561. doi: 10.1093/cercor/bh1161

Cascio, C. J., Foss-Feig, J. H., Burnette, C. P., Heacock, J. L., & Cosby, A. A. (2012). The rubber hand illusion in children with autism spectrum disorders: delayed influence of combined tactile and visual input on proprioception. *Autism, 16*, 406-419. doi: 10.1177/1362361311430404

Centelles, L., Assaiante, C., Etchegoyhen, K., Bouvard, M., & Schmitz, C. (2013). From action to interaction: Exploring the contribution of body motion cues to social understanding in typical development and in autism spectrum disorders. *Journal of Autism and Developmental Disorders, 43*, 1140-1150. doi: 10.1007/s10803-012-1655-0

Cheng, Y., Yang, C-Y., Lin, C-P., Lee, P-L., & Decety, J. (2008). The perception of pain in others suppresses somatosensory oscillations: A magnetoencephalography study. *Neuroimage, 40*, 1833-1840. doi: 10.1016/j.neuroimage.2008.01.064

Constantino, J. N., Davis, S. A., Todd, R. D., Schindler, M. K., Gross, M. M., Brophy, S. L., Metzger, L. M., Shoushtari, C. S., Splinter, R., & Reich, W. (2003). Validation of a brief quantitive measure of autistic traits: comparison of the social responsiveness scale with the autism diagnostic interview-revised. *Journal of Autism and Developmental Disorders, 33*, 427-433. doi: 10.1023/A:1025014929212

Davis, M. H. (1980). A multidimensional approach to individual differences in empathy. *JSAS Catalog of Selected Documents in Psychology, 10*, 85.

Dawson, G., & Adams, A. (1984). Imitation and social responsiveness in autistic children. Journal of abnormal child psychology, 12, 209-225. doi: 10.1007/BF00910664

Dawson, M. E., Schell, A. M., & Fillion, D. L. (2000). The electrodermal system. In J. T. Cacioppo, L. G. Tassinary & G. G. Berntson (Eds.), Handbook of psychophysiology (pp. 200-224). Cambridge: Cambridge University Press.

De Clercq, A., Verschuere, B., De Vlieger, P., & Crombez, G. (2006). Psychophysiological Analysis (PSPHA): A modular script-based program for analyzing psychophysiological data. *Behavior Research Methods, 38*, 504-510. doi: 10.3758/BF03192805

De Coster, L., Verschuere, B., Goubert, L., Tsakiris, M., & Brass, M. (2013). I suffer more from your pain when you act like me: Being imitated enhances affective responses to seeing someone else in pain. *Cognitive, Affective, & Behavioral Neuroscience, 13*, 519-532. doi: 10.3758/s13415-013-0168-4

Dinstein, I., Thomas, C., Humpreys, K., Minshew, N., Behrmann, M., & Heeger, D. J. (2010). Normal movement selectivity in autism. *Neuron, 66*, 461-469. doi: 10.1016/j.neuron.2010.03.034

Escalona, A., Field, T., Nadel, J., & Lundy, B. (2002). Brief report: Imitation effects on children with autism. *Journal of autism and developmental disorders, 32*, 141-144.

Fan, Y.-T., Chen, C., Chen, S.-C., Decety, J., & Cheng, Y. (2013). Empathic arousal and social understanding in individuals with autism: evidence from fMRI and ERP measurements. *Social, Cognitive, and Affective Neuroscience*, published online. doi: 10.1093/scan/nst101

Field, T., Field, T., Sanders, C., & Nadel, J. (2001). Children with autism display more social behaviors after repeated imitation sessions. *Autism, 5*, 317-323. doi: 0185901362-3613(200109)5

Funayama, E. S., Grillon, C., Davis, M., & Phelps, E. A. (2001). A double dissociation in the affective modulation of startle in humans: Effects of unilateral temporal lobectomy. *Journal of Cognitive Neuroscience, 13*, 721-729. doi: 10.1162/08989290152541395

Gallese, V., & Sinigaglia, C. (2011). What is so special about embodied simulation? *Trends in Cognitive Sciences, 15*, 512-519. doi: 10.1016/j.tics.2011.09.003

Gazzola, V., Aziz-Zadeh, L., & Keysers, C. (2006). Empathy and the somatotopic auditory mirror system in humans. *Current Biology, 16*, 1824-1829. doi: 10.1016/j.cub.2006.07.072

Gonzalez-Liencres, C., Shamay-Tsoory, S. G., & Brüne, M. (2013). Towards a neuroscience of empathy: ontogeny, phylogeny, brain mechanisms, context and psychopathology. *Neuroscience and Biobehavioral Reviews, 37*, 1537-1548. doi: 10.1016/j.neurobiorev.2013.05.001

Hadjikhani, N., Zürcher, N. R., Rogier, O., Hippolyte, L., Lemonnier, E., Ruest, T., Ward, N., Lassalle, A., Gillberg, N., Billstedt, E., Helles, A., Gillberg, C., Solomon, P., Prkachin, K. M., & Gillberg, C. (2014). Emotional contagion for pain is intact in autism spectrum disorders. *Translational Psychiatry (e343).* doi: 10.1038/tp.2013.113

Hawk, L. W., & Cook, E. W. (2000). Independence of valence modulation and prepulse inhibition of startle. *Psychophysiology,37*, 5-12. doi: 10.1111/1469-8986.3710005

Hamilton, A. F. (2013). Reflecting on the mirror neuron system in autism: A systematic review of current theories. *Developmental Cognitive Neuroscience, 3*, 91-105. doi: 10.1016/j.dcn.2012.09.008

Kaplan, J. T., & Iacoboni, M. (2006). Getting a grip on other minds: Mirror neurons, intention, understanding, and cognitive empathy. *Social Neuroscience, 1*, 175-183. doi: 10.1080/17470910600985605

Keysers, C., Kaas, J. H., & Gazzola, V. (2010). Somatosensation in social perception. *Nature Reviews Neuroscience, 11*, 417-428. doi: 10.1038/nrn2833

Lamm, C., Nusbaum, H. C., Meltzoff, A. N., & Decety, J. (2007). What are you feeling? Using functional magnetic resonance imaging to assess the modulation of sensory and affective responses during empathy for pain. *PloS One, 12*: e 1292. doi: 10.1371/journal.pone.0001292

Loggia, M. L., Mogil, J. S., & Bushnell, M. C. (2008). Empathy hurts: Compassion for another increases both sensory and affective components of pain perception. *Pain, 136*, 168-176. doi: 10.1016/j.pain.2007.07.017

Lombardo, M. V., Chakrabarti, B., Bullmore, E. T., MRC AIMS Consortium, & Baron-Cohen, S. (2011). Specialization of right temporo-parietal junction for mentalizing and its relation to social impairments in autism. *Neuroimage, 56*, 1832-1838. doi: 10.1016/j.neuroimage.2011.02.067

McNeil, D. W., Rainwater, A. J. (1998). Development of the Fear of Pain Questionnaire-III. *Journal of Behavioral Medicine, 21*, 389-410. doi: 10.1023/A:1018782831217

Minio-Paluello, I., Baron-Cohen, S., Avenanti, A., Walsh, V., & Aglioti, S. M. (2009). Absence of embodied empathy during pain observation in Asperger Syndrome. *Biological Psychiatry, 65*, 55-62. doi: 10.1016/j.biopsych.2008.08.006

Minshew, N. J., Turner, C. A., & Goldstein, G. (2005). The application of short forms of the Weschler Intelligence Scales in adults and children with high functioning autism. *Journal of Autism and Developmental Disorders, 35*, 45-52. doi: 10.1007/s10803-004-1030-x

Nadel, J., & Preze, A. (1993). What makes immediate imitation communicative in toddlers and autistic children? In J. Nadel & L. Camaioni (Eds.), *New perspectives in early communicative development*. London, NY: Routledge

Oberman, L. M., & Ramachandran, V. S. (2007). The simulating social mind: The role of the mirror neuron system and simulation in the social and communicative deficits of autism spectrum disorders. *Psychological Bulletin, 133*, 310-327. doi: 10.1037/0033-2909.133.2.310

Palmer, C. J., Paton, B., Hohwy, J., & Enticott, P. G. (2013). Movement under uncertainty: the effects of the rubber-hand illusion vary along the nonclinical autism spectrum. *Neuropsychologia, 51*, 1942-1951. soi: 10.1016/j.neuropsychologia.2013.06.020

Paton, B.,Hohwy, J., & Enticott, P. G. (2012). The rubber hand illusion reveals proprioceptive and sensorimotor differences in autism spectrum disorders. *Journal of Autism and Developmental Disorders, 42*, 1870-1883. doi: 10.1007.s10803-011-1430-7

Pellicano, E., & Burr, D. (2012). When the world becomes 'too real': a Bayesion explanation of autistic perception. *Trends in Cognitive Sciences, 16*, 504-510. doi: 10.1016/j.tics.2012.08.009

Poljac, E., Poljac, E., & Wagemans, J. (2013). Reduced accuracy and sensitivity in the perception of emotional facial expressions in individuals with high autism spectrum traits. *Autism, 17*, 668-680. doi: 10.1177/1362361312455703

Rizzolatti, G., & Craighero, L. (2004). The mirror-neuron system. *Annual Review of Neuroscience, 27*, 169-192. doi: 10.1146/annurev.neuro.27.070203.144230

Rizzolatti, G., & Sinigaglia, C. (2010). The functional role of the parieto-frontal mirrror circuit: interpretations and misinterpretations. *Nature Reviews Neuroscience, 11*, 264-274. doi: 10.1038/nrn2805

Rogers, K., Dziobek, I., Hassenstab, J., Wolf, O. T., & Convit, A. (2007). Who cares? Revisiting empathy in Asperger Syndrome. *Journal of Autism and Developmental Disorders, 37*, 709-715. doi: 10.1007/s10803-006-0197-8

Ruscheweyh, R., Marziniak, M., Stumpenhorst, F., Reinholz, J., & Knecht, S. (2009). Pain sensitivity can be assessed by self-rating: development and validation of the Pain Sensitivity Questionnaire. *Pain, 146*, 65-74. doi: 10.1016/j.pain.2009.06.020

Russell, J. (1997). *Autism as an executive disorder*. New York, NY: Oxford University Press.

Rutter, M. (1974). Development of infantile autism. *Psychological Medicine, 4*, 147-163. doi: 10.1017/S0033291700041982

Ruysschaert, L., Warreyn, P., Wiersema, J. R., Oostra, A., & Roeyers, H. (2014). Exploring the role of neural mirroring in children with autism spectrum disorder. *Autism Research, 7*, 197-206. doi: 10.1002/aur.1339

Schwarzkopf, S., Schilbach, L., Vogeley, K., & Timmermans, B. (2014). "Making it explicit" makes a difference: evidence for a dissociation of spontaneous and intentional level 1 perspective taking in high-functioning autism. *Cognition, 131*, 345-354. doi: 10.1016/j.cognition.2014.02.003

Senju. A. (2012). Spontaneous theory of mind and its absence in autism spectrum disorders. *Neuroscientist, 18*, 108-113. doi: 10.1177/1073858410397208

Singer, T., Seymour, B., O' Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for Pain Involves the Affective but not Sensory Components of Pain. *Science, 303*, 1157-1162. doi: 10.1126/science.1093535

Smith, A. (2006). Cognitive empathy and emotional empathy in human behavior and evolution. *Psychological Record, 56*, 3-21.

Smith, A. (2009). The empathy imbalance hypothesis of autism: a theoretical approach to cognitive and emotional empathy in autistic development. *Pscyhological Record, 59*, 489-510.

Spengler, S., Bird, G., & Brass, M. (2010). Hyperimitation of actions is related to reduced understanding of others' minds in autism spectrum conditions. *Biological Psychiatry, 15*, 1148-1155. doi: 10.1016/j.biopsych.2010.09.017

Tajadura-Jimenez, A., Grehl, S., & Tsakiris, M. (2012). The other in me: Interpersonal multisensory stimulation changes the mental representation of the self. *PLOS one, 7*. doi: 10.1371/journal.pone.0040682

van Boxtel, J. J. A., & Lu, H. (2013). A predictive coding perspective on autism spectrum disorders. *Frontiers in Psychology, 4*. doi: 10.3389/fpsyg.2013.00019

Williams, J. H. G., Whiten, A., & Singh, T. (2004). A systemic review of action imitation in autism spectrum disorder. *Journal of Autism and Developmental Disorders, 34*, 285-299. doi: 10.1023/B:JADD.0000029551.56735.3a

CHAPTER 6
GENERAL DISCUSSION

In the current thesis, we investigated whether being imitated increases reactions to observing someone else in pain. To this aim, we developed a paradigm in which subjects' finger movements are being imitated by a hand on screen or not. Subsequently, the hand on screen receives painful stimulation.

A MULTI-METHODOLOGICAL APPROACH TO INVESTIGATE THE INFLUENCE OF BEING IMITATED ON EMPATHY FOR PAIN

In four different studies using four different methodologies, we replicated the finding that being imitated modulates empathy for pain, and investigated the mechanism underlying this effect. In **Chapter 2**, we aimed to provide first evidence for the idea that being imitated increases affective responses to seeing someone else in pain using explicit behavioural and implicit psychophysiological measures. Furthermore, we wanted to explore a potential mechanism underlying this effect, with a focus on self-other overlap. In this study, both explicit and implicit responses demonstrated stronger reactions when observing another person in pain after being imitated. Moreover, by linking our paradigm to rubber hand illusion (RHI) setups we were able to show that this effect was mediated by self-other merging processes. Thus, this study established our paradigm as a valuable tool to investigate our research question, and provided important first insights into the effect.

In a transcranial magnetic stimulation (TMS) study (**Chapter 3**) motor evoked potentials (MEPs) were induced in the first dorsal interroseus (FDI) of the right hand when observing pain after being imitated. This way, we aimed to investigate whether being imitated not only affects automatic emotional responses, but whether it also has an effect on specific action tendencies, testing how far the consequences of being imitated on empathy for pain extended. We were able to show that our imitation manipulation had different effects on bodily action tendencies. While not being imitated induced a decrease of corticospinal excitability (CSE; in accordance with previous literature; e.g. Avenanti, Bueti, Galati, & Aglioti, 2005; Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2006), being imitated resulted in an increase of CSE. These findings were able to account for previously observed contradicting findings (Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2009; Fitzgibbon et al., 2012), by positing that CSE changes when observing someone else in pain are dependent upon the control participants can exert over the pain they see. When not exerting control (not being imitated), the most adaptive response is to show an anaesthetic inhibition response, while exerting control (being imitated) provides the opportunity to prepare for a withdrawal response. As such, with this TMS study we demonstrated that our imitation manipulation can influence action tendencies in a specific manner, providing important insight into existing discrepancies in the literature, and showing the power of our manipulation.

In **Chapter 4**, functional magnetic resonance imaging (fMRI) was used to directly examine which brain areas become more active when observing someone else in pain after being imitated. More specifically, we wanted to investigate which parts of the pain matrix (affective or sensory; see Lamm, Decety, & Singer, 2011; Singer et al., 2004) are influenced by being imitated. Moreover, this study allowed to provide first neural evidence

for the idea that self-other overlap underlies the effect of being imitated on empathy for pain, by looking at modulation of neural structures related to self-other merging by our imitation manipulation. When looking at activation during observation of pain after being imitated, peak activity was found in the dorsal anterior insula (AI) and right temporo-parietal junction (TPJ). These activations were interpreted as reflecting heightened affective states (Lamm et al., 2011) and self-other overlap (Brass, Zysset, & von Cramon, 2001; Brass, Ruby, & Spengler, 2009; Spengler, Bird, & Brass, 2010) respectively. Furthermore, since the dorsal AI has been related to motor control and translation of emotional states into action tendencies (Lamm & Singer, 2010), these results were complementary to our TMS study that showed specific action tendencies when being imitated. With this fMRI experiment we were thus able to provide compelling neural evidence for the idea that being imitated increases activation in specific areas of the pain matrix when observing pain, and support the idea that self-other confusion plays an important role.

Finally, in **Chapter 5** the aforementioned paradigm was applied to adults with high functioning autism (HFA). A large number of studies suggest deficiencies in imitation and empathy abilities, although consensus on these deficiencies seems difficult to reach (e.g. Williams, Whiten, & Sing, 2004 versus Spengler et al., 2010 for imitation and Baron-Cohen & Wheelwright, 2004 versus Hadjikhani et al., 2014 for empathy). Since the current paradigm encompasses both processes, our paradigm provided us with a valuable tool to gain more insight into these findings by investigating whether and how the effect of being imitated on empathy for pain is different in adults with HFA. First, no overall empathy differences between HFA and typically developing (TD) adults were observed (on implicit and explicit measures). However, the influence of being imitated on empathy for pain in

HFA seemed to show a different pattern than that of TD. In the beginning of the experiment, lower affective responses after being imitated were observed, while higher affective responding was observed at the end of the experiment (replicating findings of TD adults). Importantly, this study showed that individuals with HFA are able to show empathy, and that being imitated can influence this empathic response, albeit in a different manner from that of TD controls. Rather than supporting a dysfunctional MNS hypothesis (Williams et al., 2004), these findings were interpreted as evidence for a deficit in the control of merging between self and other in ASD (Spengler et al., 2010; see also Hamilton, 2013).

SELF-OTHER CONFUSION AND THE INFLUENCE OF BEING IMITATED ON EMPATHY FOR PAIN

Thus, in four studies we were able to provide compelling evidence for the idea that being imitated influences observing someone else in pain. A second aim of this thesis comprised of investigating the process underlying this effect. Research has suggested that imitation is based on a mechanism that directly matches the observed action onto a corresponding motor representation in the observer (motor simulation; Brass & Heyes, 2005; Iacoboni et al., 1999). Furthermore, a similar process seems to take place for emotions and affective states, suggesting embodied simulation (Bastiaansen, Thioux, & Keysers, 2009; Heberlein & Atkinson, 2009). More specifically, research on empathy for pain indicates that observed and experienced pain share neural structures (Singer et al., 2004, for a meta-analysis see Lamm et al., 2011). Thus, both imitation and empathy for pain have been linked to sharing of representations between self and other, although they have – thus far – not been related to one another. In the current thesis, however, we have

repeatedly found evidence for the idea that being imitated increases self-other confusion and as a result leads to higher empathy for pain. In the first study, we linked our paradigm to RHI setups (Botvinick & Cohen, 1998) by creating a setup that resembles an action induced RHI (Dummer, Picot-Annand, Neal, & Moore, 2009), and showing that the influence of being imitated on empathy or pain is mediated by this illusion. Since this paradigm has also been strongly linked to sharing of representations between self and other (Tajadura-Jiménez, Grehl, & Tsakiris, 2012), this study provided the first evidence for the idea that self-other overlap underlies the effect of being imitated on empathy for pain. Furthermore, our TMS study indicated that the imitation manipulation modulated action tendencies when observing someone else in pain, suggesting that the self is strongly affected. Being imitated led to an increase of CSE when observing pain, suggesting preparation for withdrawal. Such a withdrawal only makes sense if confusion between self and other takes place, since own bodily reactions are affected. Importantly, our fMRI study was the first to explicitly show involvement of the TPJ (a region linked to self-other overlap; Brass et al., 2001; Brass et al., 2009; Spengler et al., 2010) in the paradigm, providing a first direct indication for the involvement of self-other merging as an important process. Moreover, our study with adults with HFA suggested that being imitated has an effect on empathy for pain, albeit in a different manner for HFA compared to TD adults, suggesting deficiencies with the self-other overlap process underlying the effect. More specifically, the reversal of effects over time indicated that a deficient control over this self-other merging was responsible for the effects found in HFA. Finally, it has to be noted that – due to the randomization of the imitative and non-imitative blocks in the setup – we demonstrated that being imitated influences empathy for pain on a trial-by-trial basis, which seems at odds with an

account that would assume that being imitated induces a general prosocial liking (van Baaren, Holland, Kawakami, & van Knippenberg).Thus, all these data support the idea that self-other confusion plays an important role in the current paradigm rather than a mere abstract affiliation with the other person, providing insights into mechanisms possibly important in other social interactions. However, an essential question that comes to mind when having a close look at the paradigm and assuming self-other confusion is whether the current thesis genuinely investigates 'being imitated' rather than exerting control over an observed hand. There are several important differences between the current paradigm and social-psychological research on being imitated. Due to the absence of a delay between executed and observed movements, the basic simplicity of these movements, and the usage of a first person perspective, the imitative versus non-imitative situation was immediately transparent to participants. While this was explicitly done in order to increase self-other overlap, this limits the ecological validity of the effects. Social-psychological research has indicated, for example, that complex prosocial effects of being imitated only take place when subjects are unaware of the imitative situation (Chartrand & Bargh, 1999; van Baaren et al., 2004). Thus, it is not straightforward that more complex social situations operate in a similar fashion, although it seems peculiar that self-other confusion would not extent its influence to these situations as well.

EMPATHY FOR PAIN VERSUS EMOTIONAL CONTAGION?

Another important question arises when assuming that confusion between self and other is the core mechanism responsible for our effects. While empathy has been defined as' the ability to share the affective experiences of others' (Singer & Lamm, 2009), literature suggest that this

empathic response requires the ability to experience feelings of the other person while at the same time being able to recognize this person as different from the self (see Singer and Lamm, 2009 for an overview of terminology). As such, it is disputable whether the term 'empathy for pain' is still applicable to the current paradigm. As shown in the first behavioural study, we demonstrated that indices of the RHI such as agency, control and body ownership were higher in the imitation condition. As a matter of fact, it was exactly this assumption that allowed us to conduct the TMS study, which showed that our imitation manipulation had strong implications for the self (modulating bodily action tendencies). Furthermore, our fMRI study clearly indicated activity in the TPJ, a region strongly linked to self-other distinction (Brass et al., 2001; Brass et al., 2009; Spengler et al., 2010), during empathy for pain after being imitated. This suggest a stronger need for distinction in this situation and again indicates a reduction of boundaries between self and other. It is therefore an open question whether it is empathy or rather agency mechanisms that allow us to share emotions in the current paradigm. Ehrsson, Wiech, Welskopf, Dolan, & Passingham (2007), for example, have demonstrated that threatening a rubber hand that feels as if it is your own hand increases brain activity in pain-related brain areas such as the ACC and AI. Thus, our paradigm – strongly linked to the RHI as well – activates similar neural structures as observed when conducting RHI experiments. However, although all implicit results strongly indicate that a self-other confusion mechanism takes place, it cannot be excluded that other processes are present as well. Ratings on our behavioural self-report questions suggested that people still consciously seem to distinguish self from other. Responses to other- and self-related questions were differently rated, with higher scores on other-related than on self-related subjective judgments. This suggests that self-other confusion was not complete, since a clear distinction

between self and other still seemed obvious to participants. We therefore opted to use the term empathy for pain throughout the thesis nevertheless, although it should be noted that this term might not encompass the whole process. The question remains whether reactions in the current paradigm were about the other (empathy for pain) or about the self (emotional contagion).

IMPLICIT VERSUS EXPLICIT MEASURES OF EMPATHY FOR PAIN

Another important aspect of the current paradigm is the apparent absence of any relationship between explicit and implicit measures. In all four studies, no correlation between explicit (self-reports) and implicit (psychophysiology, MEPs, brain activation) responses was observed. However, this need not be surprising, since several accounts suggest a dissociation between emotional and cognitive empathy (Hynes, Baird, & Grafton, 2006; Schulte-Ruther, Markowitsch, Fink, & Piefke, 2007; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009; Vollm et al., 2006). Shamay-Tsoory et al. (2009) suggest that the inferial frontal gyrus (IFG) structure is necessary for affective empathy, while the ventromedial prefrontal cortex (vMPFC) is responsible for cognitive empathy. While the affective system is related to the mirror neuron system (MNS), the cognitive system is thought to be more related to theory of mind (TOM) and mentalizing abilities. The relationship between these two forms of empathy, however, and their possible interaction is still a matter of debate. Thus, if our explicit measures would tap into the cognitive system while implicit measures activate the emotional system, the link between both responses remains to be investigated. The first behavioural study, the TMS and fMRI study all show similar effects for explicit and implicit measures, suggesting

at least a partial overlap and possible presence of similar underlying mechanisms. However, the study with adults with HFA showed a distinction when looking at effects of being imitated on explicit versus implicit responses for HFA, suggesting that a clear dissociation is present as well. One possibility would be that both measures tap into the different mechanisms mentioned above. Thus, explicit responses might be more related to abstract empathy and increased liking, since behavioural self-reports suggested that self from other were still clearly distinguishable. Implicit measures, on the other hand, might be more prone to self-other confusion. An interesting follow-up would be to investigate whether explicit prosocial rating generalize to other people not involved in the initial interaction (see e.g. van Baaren et al., 2004), while implicit responses are focused on the direct interaction partner with whom self-other overlap takes place.

CONCLUSIONS AND FUTURE DIRECTIONS

In sum, in a series of four studies, we have shown that being imitated increases reactions to observing someone else in pain. Providing evidence for a shared representational account underlying these effects, we demonstrate that a basic mechanism allows for the interaction between the motor system serving imitation and the sensory system responsible for simulating observed pain. A few important questions, however, remain unanswered. As mentioned above, an important issue is whether the current paradigm investigates control rather than being imitated, and which similarities or discrepancies with the RHI are present. Thus, it is necessary to explore whether more ecologically valid social imitation interactions operate in similar ways. More specifically, it would be interesting to investigate

whether self-other overlap is an important process in more complex social situations as well. Thus, it is clear that our operationalization of being imitated shows discrepancies with daily social interactions in naturalistic environments. Related to this, the temporal contingency that is present in both experimental conditions in our setup (being imitated and not being imitated) also forces us to think whether the current paradigm was more about contingency rather than imitation. Creating a setup in which contingency and imitation are dissociated would be highly interesting since it would allow us to look at situations in which complete control is present without being imitated, and possibly distinguish positive effects of being imitated from negative effects of not being imitated. Although all these setup-related limitations are recognized, we nevertheless believe that the current thesis has provided important understanding into social (imitative) interactions and observation of others in pain, combining two fields of study that were previously unrelated.

REFERENCES

Avenanti, A., Bueti, D., Galati, D., & Aglioti, S. M. (2005). Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nature Neuroscience, 8*, 955-960. doi: 10.1038/m1481

Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2006). Stimulus-driven modulation of motor-evoked potentials during observation of others' pain. *Neuroimage, 32*, 316-324. doi: 10.1016/j.cortex.2008.10.004

Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2009). The pain of a model in the personality of an onlooker: Influence of state-reactivity and personality traits on embodied empathy for pain. *Neuroimage, 44*, 275-283. doi: 10.1016/j.neuroimage.2008.08.001

Baron-Cohen, S., & Wheelwright, S. (2004). The empathy quotient: an investigation of adults with Asperger syndrome or high functioning, and normal sex differences. *Journal of Autism and Developmental Disorders, 34*, 163-175. doi: 10.1023/B:JADD.0000022607.19833.00

Bastiaansen, J. A. C. J., Thioux, M., & Keysers, C. (2009). Evidence for mirror systems in emotions. *Philophical Transactions of the Royal Society B – Biological Sciences, 364*, 2391-2404. doi: 10.1098/rstb.2009.0058

Botvinick, M., & Cohen, J. (1998). Rubber hands 'feel' touch that eyes see. *Nature, 391*, 756- 756. doi:10.1038/35784

Brass, M., & Heyes, C. (2005). Imitation: Is cognitive neuroscience solving the correspondence problem? *Trends in Cognitive Sciences, 9*, 489-495. doi: 10.1016/j.tics.2005.08.007

Brass, M., Ruby, P., & Spengler, S. (2009). Inhibition of imitative behaviour and social cognition. *Philosophical Transactions of the Royal Society B-Biological Sciences, 364*, 2359-2367. doi: 10.1098/rstb.2009.0066

Brass, M., Zysset, S., & von Cramon, D. Y. (2001). The inhibition of imitative response tendencies. *Neuroimage, 14*, 1416-1423. doi: 10.1006/nimg.2001.0944

Chartrand, T. L., & Bargh, J. A. (1999). The Chameleon effect: The perception-behaviour link and social interaction. *Journal of Personality and Social Psychology, 76*, 893-910. doi: 10.1037/0022-3514.76.6.893

Fitzgibbon, B. M., Enticott, P. G., Bradshaw, J. L., Giummarra, M. J., Chou, M., Georgiou-Karistianis, N., & Fitzgerald, P. B. (2012). Enhanced corticospinal response to observed pain in pain synesthetes. *Cognitive, Affective, & Behavioral Neuroscience, 12*, 406-418. doi: 10.3758/s13415-011-0080-8

Dummer, T., Picot-Annand, A., Neal, T., & Moore, C. (2009). Movement and the rubber hand illusion. *Perception, 38*, 271-280. doi: 10.1068/p5921

Ehrsson, H. H., Wiech, K., Welskopf, N., Dolan, R. J., & Passingham, R. E. (2007). Threatening a rubber hand that you feel is yours elicits a cortical anxiety response. *Proceedings of the National Academy of Sciences in the United States of America, 104*, 9828-9833, doi: 10.1073/pnas.0610011104

Hadjikhani, N., Zürcher, N. R., Rogier, O., Hippolyte, L., Lemonnier, E., Ruest, T., Ward, N., Lassalle, A., Gillberg, N., Billstedt, E., Helles, A., Gillberg, C., Solomon, P., Prkachin, K. M., & Gillberg, C. (2014). Emotional contagion for pain is intact in autism spectrum disorders. *Translational Psychiatry (e343).* doi: 10.1038/tp.2013.113

Hamilton, A. F. (2013). Reflecting on the mirror neuron system in autism: A systematic review of current theories. *Developmental Cognitive Neuroscience, 3*, 91-105. doi: 10.1016/j.dcn.2012.09.008

Heberlein, A. S., & Atkinson, A. P. (2009). Neuroscientific evidence for simulation and shared substrates in emotion recognition. *Emotion Review, 1*, 162-177. doi: 10.1177/1754073908100441

Hynes, C. A., Baird, A. A., & Grafton, S. T. (2006). Differential role of the orbitofrontal lobe in emotional versus cognitive perspective-taking. *Neuropsychologia, 44*, 374-383. doi: 10.1016/j.neuropsychologia.2005.06.011

Iacoboni, M., Woods, R. P., Brass, M., Bekkering, H., Mazziotta, J. C., & Rizzolatti, G. (1999). Cortical mechanisms of human imitation. *Science, 286*, 1526-2538. doi: 101126/science.286.5449.2526

Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage, 54*, 2492-2502. doi: 10.1016/j.neuroimage.2010.10.014

Lamm, C., & Singer, T. (2010). The role of the anterior cingulate cortex in social emotions. *Brain Structure & Function, 214*, 579-591. doi: 10.1007/s00429-010-0251-3

Schulte-Ruther, M., Markowitsch, H. J., Fink, G. R., & Piefke, M. (2007). Mirron neuron and theory of mind mechanisms involve face-to-face interactions: a functional magnetic resonance imaging approach to empathy. *Journal of Cognitive Neuroscience, 19*, 1354-1372. doi: 10.1162/jocn.2007.19.8.1354

Shamay-Tsoory, S. G., Aharon-Peretz, J., & Perry, D. (2009). Two systems for empathy: a double dissociation between emotional and cognitive empathy in inferior frontal gyrus versus ventromedial prefrontal lesions. *Brain, 132*, 617-627. doi: 10.1093/brain/awn279

Singer, T., & Lamm, C . (2009). The Social Neuroscience of Empathy. *Annals of the New York Academy of Sciences, 1156*, 81-96. doi: 10.1111/j.1749-6632.2009.04418.x

Singer, T., Seymour, B., O' Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for Pain Involves the Affective but not Sensory Components of Pain. *Science, 303*, 1157-1162. doi: 10.1126/science.1093535

Spengler, S., Bird, G., & Brass, M. (2010). Hyperimitation of actions is related to reduced understanding of others' minds in autism spectrum conditions. *Biological Psychiatry, 15*, 1148-1155. doi: 10.1016/j.biopsych.2010.09.017

Tajadura-Jimenez, A., Grehl, S., & Tsakiris, M. (2012). The other in me: Interpersonal multisensory stimulation changes the mental representation of the self. *PLOS one, 7*. doi: 10.1371/journal.pone.0040682

van Baaren, R. B., Holland, R. W., Kawakami, K., & van Knippenberg, A. (2004). Mimicry and Prosocial Behavior. *Psychological Science, 15*, 71-74. doi: 10.1111/j.0963-7214.2004.01501012.x

Völlm, B. A., Taylor, A. N. W., Richardson, P., Corcoran, R., Stirling, J., McKie, S., Deakin, J. F. W., & Elliot, R. (2006). Neural correlates of theory of mind and empathy: a functional magnetic resonance imaging study in a nonverbal task. *Neuroimage, 29*, 90-98. doi: 10.1016/j.neuroimage.2005.07.022

Williams, J. H. G., Whiten, A., & Singh, T. (2004). A systemic review of action imitation in autism spectrum disorder. *Journal of Autism and Developmental Disorders, 34*, 285-299. doi: 10.1023/B:JADD.0000029551.56735.3a

CHAPTER 7
NEDERLANDSTALIGE SAMENVATTING

Imitatie is een belangrijk aspect van ons dagelijks leven. Onderzoek heeft aangetoond dat imitatie over, automatisch en zelfs tussen totale vreemden plaatsvindt (Brass, Bekkering, Wöhlschlager, & Prinz, 2000; Brass, Bekkering, & Prinz, 2001; Chartrand & Bargh, 1999; Lakin & Chartrand, 2003). Chartrand en Bargh (1999) toonden met het 'Chameleon effect' aan dat mimicry (non-intentionele, automatische imitatie) een invloed heeft op hoe we met anderen omgaan en anderen percipiëren: we vinden iemand die ons imiteert leuker en de interactie met deze persoon verloopt vlotter. Een brede waaier aan sociaal-psychologisch onderzoek heeft sindsdien aangetoond dat geïmiteerd worden allerlei positieve sociale gevolgen met zich meebrengt, van meer helpgedrag en generositeit naar de imitator tot een algemene prosociale oriëntatie (e.g. Kühn et al., 2010; Lakin, Chartrand, & Arkin, 2008; Stel, van Baaren, & Vonk, 2008; van Baaren, Holland, Kawakami, & van Knippenberg, 2004). Imitatie blijkt dus een essentieel proces te zijn dat relaties tussen individuen versterkt. Alhoewel al meermaals is aangetoond dat imitatie een invloed heeft op complexe sociale gedragingen is nog nooit onderzocht of geïmiteerd worden ook meer basale en automatische processen, zoals het observeren van anderen in pijn, kan beïnvloeden.

Singer et al. (2004) toonden voor het eerst aan dat het observeren van anderen in pijn gelijkaardige breinregio's activeert als wanneer personen zelf pijn ervaren (empathie voor pijn). Verschillende studies demonstreerden dat hierbij vooral de affectief-motivationele dimensies van pijn geactiveerd worden (Goubert, Vervoort, & Craig, 2012; Jackson, Meltzoff, & Decety,

2005; Lamm, Decety, & Singer, 2011; Singer et al., 2006), alhoewel steeds meer evidentie gevonden wordt voor de idee dat ook sensorische dimensies actief worden (Bufalari, Aprile, Avenanti, Di Russo, & Aglioti, 2007; Cheng, Yang, Lin, Lee, & Decety, 2008; Lamm, Nusbaum, Meltzoff, & Decety, 2007; Loggia, Mogil, & Bushnell, 2008; for a review see Keysers, Kaas, & Gazzola, 2010). Een meta-analyse van Lamm et al. (2011) demonstreerde dat vooral de anterieure insula (AI) en anterieur cingulate cortex (ACC) consistent geactiveerd worden bij pijnobservatie. Verder toonden verschillende studies reeds aan dat empathie voor pijn gemoduleerd kan worden door cognitieve top-down (e.g. Cheng et al., 2007; Decety, Echols, & Corell, 2009; de Vignemont & Singer, 2006; Hein & Singer, 2008; Lamm, Meltzoff, & Decety, 2010; Singer et al., 2006) en bottom-up invloeden (e.g. Han, Fan, & Mao, 2008; Xu, Zuo, Wang, & Han, 2009; Yang, Decety, Lee, Chen, & Cheng, 2009). De invloed van geïmiteerd worden op empathie voor pijn is echter – tot nu toe – nog nooit onderzocht.

DOELEN VAN HET ONDERZOEK

Het doel van de huidige thesis was om na te gaan of geïmiteerd worden reacties op het zien van anderen in pijn kan moduleren. Aangezien geïmiteerd worden prosociaal gedrag verhoogt (e.g. Kühn et al., 2010; Lakin et al., 2008; van Baaren et al., 2004) lijkt het intuïtief dat ook responsen op het observeren van anderen in pijn verhoogd zouden worden door imitatie. Verder wouden we in de huidige thesis eveneens onderzoeken welk(e) mechanisme(n) onderliggend zijn aan het effect van imitatie op empathie voor pijn. De focus lag hierbij op de theorie die veronderstelt dat gedeelde representaties tussen het zelf en de ander de invloed van geïmiteerd worden op empathie voor pijn mediëren. Zowel imitatie (Brass & Heyes, 2005) als

empathie voor pijn (Bastiaansen, Thioux, & Keysers, 2009; Heberlein & Atkinson, 2009) werden voorheen gelinkt aan dit idee van gedeelde representaties, maar beiden werden nog niet met elkaar verbonden. Dergelijke link zou belangrijke inzichten kunnen verschaffen in de samenwerking tussen het motorische systeem dat instaat voor imitatie en het sensorische systeem dat verantwoordelijk is voor empathie voor pijn. De voorspelling van de huidige thesis was bijgevolg dat geïmiteerd worden zelf-ander overlap zou verhogen aangezien eigen en andermans acties in een gemeenschappelijk domein gecodeerd worden (e.g. Brass, Derrfuss, Cramon, & von Cramon, 2003; Liepelt, von Cramon, & Brass, 2008). Deze verhoogde zelf-anderverwarring zou bijgevolg voor verhoogde reacties op het zien van anderen in pijn moeten leiden.

Om te onderzoeken of geïmiteerd worden empathie voor pijn verhoogt, ontwikkelden we een paradigma dat beide aspecten combineerde. In dit paradigma zitten participanten voor een computerscherm waarbij ze – willkeurige en zelf gekozen – eenvoudige vingerbewegingen moeten maken. Tegelijkertijd wordt een hand op het scherm geobserveerd die deze bewegingen ofwel imiteert, ofwel niet imiteert. Na een aantal van deze bewegingen (allemaal imitatie of niet-imitatie) wordt geobserveerd hoe de hand op het scherm pijnlijke stimulatie wordt toegediend. Tijdens en na deze pijnobservatie werden respectievelijk impliciete en expliciete reacties gemeten en werd nagegaan of geïmteerd worden deze responsen kon moduleren.

In een reeks van vier studies, gebruikmakend van vier verschillende methodologieën, werd dit paradigma gebruikt om ne te gaan of geïmiteerd worden empathie voor pijn verhoogt. In een eerste gedragsstudie werden zelfrapportage en psychofysiologie gebruikt om voor de eerste keer te onderzoeken wat gebeurt bij het observeren van pijn na imitatie. Deze studie

was de eerste demonstratie van de invloed van geïmiteerd worden op empathie voor pijn en zorgde bovendien voor de eerste evidentie dat een zelf-anderverwarringsmechanisme deze effecten moduleerde. Verder toonde deze studie ook aan dat het paradigma een waardevol instrument was om onze onderzoeksvraag verder te onderzoeken. In een tweede studie werden motor evoked potentialen (MEPn) uitgelokt via transcraniële magnetische stimulatie (TMS) om na te gaan of geïmiteerd worden ook actietendensen kan beïnvloeden. In een derde studie werd functionele magnetische beeldvorming gebruikt (fMRI) aangezien zo voor het eerst direct kon worden onderzocht of imitatie inderdaad tot verhoogde pijngerelateerde activatie leidt. Tot slot werd een studie uitgevoerd met volwassenen met hoogfunctionerend autisme (HFA). Hier werd nagegaan of de invloed van geïmiteerd worden op empathie voor pijn gelijkaardig is voor deze individuen wanneer hun reacties vergeleken werden met typisch ontwikkelende (TO) volwassenen.

EEN BEKNOPT OVERZICHT VAN DE BELANGRIJKSTE BEVINDINGEN

In **Hoofdstuk 2** werd gebruik gemaakt van expliciete zelfrapportage en impliciete psychofyiologische responsen en werd aangetoond dat geïmiteerd worden affectieve reacties op het observeren van anderen in pijn verhoogt. Zowel expliciete als impliciete reacties waren sterker bij pijnperceptie na imitatie. Verder werd ook gedemonstreerd dat zelf-anderoverlap onderliggend is aan dit effect door het paradigma te linken aan de rubberen handillusie (RHI; een illusie waarbij een rubberen hand als de eigen hand wordt gepercipieed wanneer eigen en rubberen hand simultaan aangeraakt worden; Botvinick & Cohen, 1998). Deze studie bevestigde dat het huidige paradigma gebruikt kon worden om onze onderzoeksvraag

verder te onderzoeken en genereerde belangrijke inzichten in het effect en het onderliggende mechanisme.

In **Hoofstuk 3** werd een TMS studie beschreven waarbij MEPn geïnduceerd werden in de rechterhand van proefpersonen terwijl de hand op het scherm in pijn werd geobserveed. Op deze manier kon worden nagegaan of imitatie niet enkele affectieve automatische responsen beïnvloedt, maar ook specifieke actietendensen kan moduleren. In dit experiment werd aangetoond dat geïmiteerd worden inderdaad een effect heeft op dergelijke actietendsen. Terwijl niet geïmiteerd worden zorgt voor een daling in corticospinale excitabiliteit (CSE; Avenanti, Bueti, Galati, & Aglioti, 2005; Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2006), zorgt geïmiteerd worden voor een stijging in CSE (Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2009; Fitzgibbon et al., 2012). Deze resultaten waren in staat om tegenstrijdige bevindingen in de literatuur te verklaren, door ervan uit te gaan dat CSE veranderingen bij het obsveren van pijn afhankelijk zijn van de controle die men uitoefent over de hand in pijn. Wanneer geen controle aanwezig is (niet-imitatie), is een anaesthetische inhibitie de meest adaptieve respons, terwijl controle (imitatie) toelaat om het lichaam voor te bereiden op een terugtrekrespons. Deze TMS studie toonde bijgevolg aan dat onze imitatiemanipulatie verreikende consequenties had, aangezien actietendensen op een specifieke manier werden beïnvloed. Verder werden ook belangrijke inzichten verworven in bestaande discrepanties in de literatuur.

In **Hoofdstuk 4** werd gebruik gemaakt van fMRI om op een directe manier te onderzoeken welke breinregio's meer geactiveerd worden wanneer anderen in pijn worden geobserveerd na imitatie. We wouden specifiek nagaan welke delen van de pijnmatrix (affectief of sensorisch; zie Lamm et al., 2011; Singer et al., 2004) beïnvloed werden door onze

imitatiemanipulatie. Via deze studie was het ook mogelijk om neurale evidentie te bieden voor de idee dat zelf-anderoverlap een belangrijke rol speelt in huidg paradigma door na te gaan of regio's gelinkt aan zelf-anderverwarring gemoduleerd werden door de imitatiemanipulatie. Wanneer pijn werd geobserveed na imitatie, werd in huidige studie verhoogde activatie gevonden in de dorsale AI en rechtse temporo-pariëtale junctie (TPJ). Deze activaties werden geïnterpreteerd als verhoogde affectiviteit (Lamm et al., 2011) en zelf-ander distinctie (Brass, Zysset, & von Cramon, 2001; Brass, Ruby, & Spengler, 2009; Spengler, Bird, & Brass, 2010) respectievelijk. Met deze fMRI studie werd bijgevolg overtuigende evidentie geboden voor de idee dat geïmiteerd worden pijngerelateerde activatie verhoogt bij het observeren van anderen in pijn en voor de idee dat zelf-anderoverlap een belangrijke rol speelt.

Tot slot werd in **Hoofdstuk 5** het paradigma toegepast bij volwassenen met HFA. Verschillende studies toonden aan dat autismespectrumstoornissen (ASS) gepaard gaan met imitatie- en empathieproblemen. Er bestaat echter geen consensus omtrent de aard van deze problemen (e.g. Williams, Whiten, & Sing, 2004 versus Spengler et al., 2010 voor imitatie en Baron-Cohen & Wheelwright, 2004 versus Hadjikhani et al., 2014 voor empathie). Aangezien het huidige paradigma beide processen omvat, werd dit paradigma gebruikt om verdere inzichten te verwerven in deze discrepanties door na te gaan of en hoe de invloed van geïmiteerd worden op empathie voor pijn verschillend is voor HFA wanneer vergeleken werd met TO volwassenen. Er werd voor HFA een invloed van imitatie geobserveerd, maar deze invloed verschilde van diegene die geobserveerd werd voor TO. In het begin van het experiment vertoonden HFA lagere affectieve responsen na imitatie, terwijl op het einde hogere reacties werden geboserveed bij pijnperceptie. TO volwassenen repliceerden

telkens voorgaande effecten. Deze studie toonde aan dat volwassenen met HFA in staat zijn om empathische responsen te vertonen, maar dat imitatie een verschillende invloed heeft op dit empathisch functioneren in vergelijking met TO volwassnenen. De bevinding dat de invloed van geïmiteerd worden veranderd over de tijd werd geïnterpreteerd als evidentie voor een probleem in de controle van zelf-anderoverlap (Spengler et al., 2010; zie ook Hamilton, 2013).

IMPLICATIES VAN DE ONDERZOEKSRESULTATEN

Met behulp van bovenstaande vier hoofdstukken waren we in staat overtuigende evidentie te bieden voor de idee dat geïmiteerd worden een invloed heeft op het observeren van anderen in pijn. Verder werd ook aangetoond dat zelf-anderoverlap onderliggend is aan dit effect. Het blijft echter onzeker of dergelijke zelf-anderverwarring ook optreedt in meer complexe sociale situaties. Het huidige paradigma vertoont belangrijke verschillen met meer ecologisch valide imitatiesituaties (geen delay tussen eigen en geobserveerde bewegingen, eenvoudige bewegingen, eerste persoon perspectief) zoals vaak gebruikt in sociaal-psychologisch onderzoek. Dergelijk onderzoek heeft immers aangetoond dat complexe prosociale gevolgen van imitatie enkel optreden indien subjecten zich niet bewust zijn van de imitatiesituatie (Chartrand & Bargh, 1999; van Baaren et al., 2004). Het is bijgevolg niet vanzelfsprekend dat ook in deze complexe sociale situaties dezelfde mechanismen optreden als in huidg paradigma. Het zou echte verbazend zijn indien ook hier niet een vorm van zelf-anderverwarring zou spelen.

Een belangrijke vraag die hierbij wordt opgeroepen is de vraag of de term ‘empathie voor pijn’ correct is bij het beschrijven van huidige effecten.

Empathie wordt immers gedefinieerd als ‘de vaardigheid om affectieve ervaringenvan anderen te delen, waarbij ook een duidelijk onderscheid tussen zelf en ander aanwezig blijft’ (Singer & Lamm, 2009). Alle studies wezen op de idee dat zelf-anderverwarring de grenzen tussen zelf en ander vervaagde. In de eerste studie werd immers aangetoond dat RHI indices zoals agency, controle en lichaamseigenschap verhoogd waren in de imitatieconditie. Deze assumptie was dan ook de aanleiding voor de TMS studie, waarin getoond werd dat onze imitatiemanipulatie in staat was actietendensen te moduleren. Dit was opnieuw evidentie voor de idee dat imitatie een sterke invloed had op het zelf, aangezien een terugtrekrespons enkel zinvol is indien de grenzen tussen zelf en ander vervagen. Onze fMRI studie demonstreerde aanvullend dat de TPJ, een regio gelinkt aan zelf-anderdistincite (Brass et al., 2001; Brass et al., 2009; Spengler et al., 2010) geactiveerd werd tijdens pijnperceptie na imitatie, wat wijst op een sterkere nood aan het onderscheiden tussen zelf en ander in deze situatie. Het blijft dus een open vraag of in huidig paradigma empathie onderzocht werd of eerder mechanismen gerelateerd aan agency, controle en de RHI. Echter, onze gedragsresultaten toonden aan dat proefpersonen nog altijd in staat waren de ander van het zelf te onderscheiden. Zelfrapportageratings waren verschillend voor zelf- en andergerelateerde items, met significant hogere scores op items gericht op gevoelens van de ander. We opteerden er bijgevolg voor om nog steeds de term empathie voor pijn te hanteren, met het besef dat deze term hoogstwaarschijnlijk niet alle processen omvat. Het is echter noodzakelijk om na te gaan of meer ecologisch valide imitatiesituaties gelijkaardige effecten vertonen en of zelf-anderverwarring ook hier optreedt.

Tot slot moet hierbij worden opgemerkt dat de discrepantie tussen expliciete (zelfrapportage) en impliciete maten (psychofysiologie, TMS,

fMRI) in alle hoofdstukken erop zouden kunnen wijzen dat meerdere mechanismen meespelen. In geen van alle studies waren beide maten gecorreleerd, eventueel wijzend op de idee dat expliciete maten meer beïnvloed werden door een abstract empathieproces, terwijl impliciete maten gevoelig waren voor zelf-anderverwarring. Verschillende studies wezen reeds op een belangrijk onderscheid tussen cognitieve en emotionele empathie (Hynes, Baird, & Grafton, 2006; Schulte-Ruther, Markowitsch, Fink, & Piefke, 2007; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009; Vollm et al., 2006). De relatie tussen beide vormen blijft echter onduidelijk, waardoor ook de link tussen beide responsen in de huidige thesis verder onderzoek vraagt. Het zou bijvoorbeeld interessant zijn om na te gaan of expliciete maten generaliseren naar anderen niet initieel aanwezig in de sociale interactie (zie e.g. van Baaren et al., 2004), terwijl impliciete maten gefocused zijn op de interactiepartner met wie zelf-anderverwarring optreedt.

Kortom boden we in huidige thesis met vier studies – gebruikmakend van vier verschillende methodologieën – evidentie voor de idee dat geïmiteerd worden reacties verhoogt bij het observeren van anderen in pijn. Er werd evidentie geboden voor de idee dat gedeelde representaties tussen zelf en ander onderliggend waren aan de effecten, waardoor werd aangetoond dat een basaal mechanisme instaat voor de interactie tussen het motorische systeem (imitatie) en sensorische systeem (pijnobservatie). Alhoewel de huidige setup te maken heeft met enkele erkende limitaties, geloven we niettemin dat de huidge thesis belangrijke inzichten verschaft in allerhande sociale (imitatieve) situaties en pijnobservatie, waarbij twee – voordien ongerelateerde – onderzoeksdomeinen met elkaar verbonden werden.

REFERENTIES

Avenanti, A., Bueti, D., Galati, D., & Aglioti, S. M. (2005). Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nature Neuroscience, 8*, 955-960. doi: 10.1038/m1481

Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2006). Stimulus-driven modulation of motor-evoked potentials during observation of others' pain. *Neuroimage, 32*, 316-324. doi: 10.1016/j.cortex.2008.10.004

Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2009). The pain of a model in the personality of an onlooker: Influence of state-reactivity and personality traits on embodied empathy for pain. *Neuroimage, 44*, 275-283. doi: 10.1016/j.neuroimage.2008.08.001

Baron-Cohen, S., & Wheelwright, S. (2004). The empathy quotient: an investigation of adults with Asperger syndrome or high functioning, and normal sex differences. *Journal of Autism and Developmental Disorders, 34*, 163-175. doi: 10.1023/B:JADD.0000022607.19833.00

Bastiaansen, J. A. C. J. Thioux, M., & Keysers, C. (2009). Evidence for mirror systems in emotions. *Philosophical Transactions of the Royal Society B – Biological Sciences, 364*, 2391-2404. doi: 10.1098/rstb.2009.0058

Botvinick, M., & Cohen, J. (1998). Rubber hands 'feel' touch that eyes see. *Nature, 391*, 756- 756. doi:10.1038/35784

Brass, M., Bekkering, H., Wohlschläger, A., & Prinz, W. (2000). Compatibility between Observed and Executed Finger Movements: Comparing Symbolic, Spatial, and Imitative Cues. *Brain and Cognition, 44*, 124-143. doi: 10.1006/brcg.2000.1225

Brass, M., Bekkering, H., & Prinz, W. (2001). Movement observation affects movement execution in a simple response task. *Acta Psychologica, 106*, 3-22. doi: 10.1016/S0001-6918(00)00024-X

Brass, M., Derrfuss, J., Cramon, G. M. V., & von Cramon, D. Y. (2003). Imitative response tendencies in patients with frontal brain lesions. *Neuropsychology, 17*, 265-271. doi: 10.1037/0894-4105.17.2.265

Brass, M., & Heyes, C. M. (2005). Imitation: Is cognitive neuroscience solving the correspondence problem? *Trends in Cognitive Science, 9*, 489-495. doi: 10.1016/j.tics.2005.08.007

Brass, M., Ruby, P., & Spengler, S. (2009). Inhibition of imitative behaviour and social cognition. *Philosophical Transactions of the Royal Society B-Biological Sciences, 364*, 2359-2367. doi: 10.1098/rstb.2009.0066

Brass, M., Zysset, S., & von Cramon, D. Y. (2001). The inhibition of imitative response tendencies. *Neuroimage, 14*, 1416-1423. doi: 10.1006/nimg.2001.0944

Bufalari, I., Aprile, T., Avenanti, A., Di Russo, F., & Aglioti, S. M. (2007). Empathy for pain and touch in the human somatosensory cortex. *Cerebral Cortex, 17*, 2553-2561. doi: 10.1093/cercor/bh1161

Chartrand, T. L., & Bargh, J. A. (1999). The Chameleon effect: The perception-behaviour link and social interaction. *Journal of Personality and Social Psychology, 76*, 893-910. doi: 10.1037/0022-3514.76.6.893

Cheng, Y., Lin, C-P., Liu, H-L., Hsu, Y-Y., Lim, K-E., Hung, D., & Decety, J. (2007). Expertise modulates the perception of pain in others. *Current Biology, 17*, 1708-1713. doi: 10.1016/j.cub.2007/09/020

Cheng, Y., Yang, C-Y., Lin, C-P., Lee, P-L., & Decety, J. (2008). The perception of pain in others suppresses somatosensory oscillations: A magnetoencephalography study. *Neuroimage, 40*, 1833-1840. doi: 10.1016/j.neuroimage.2008.01.064

Decety, J., Echols, S. C., & Correll, J. (2009). The blame game: the effect of responsibility and social stigma on empathy for pain. *Journal of Cognitive Neuroscience, 22*, 985-997. doi: 10.1162/jocn.2009.21266

de Vignemont, F., & Singer, T. (2006). The emapthic brain: How, when, and why? *Trends in Cognitive Sciences, 10*, 435-441. doi: 10.1016/j.tics.2006.08.008

Fitzgibbon, B. M., Enticott, P. G., Bradshaw, J. L., Giummarra, M. J., Chou, M., Georgiou-Karistianis, N., & Fitzgerald, P. B. (2012). Enhanced corticospinal response to observed pain in pain synesthetes. *Cognitive, Affective, & Behavioral Neuroscience, 12*, 406-418. doi: 10.3758/s13415-011-0080-8

Goubert, L., Vervoort, T., & Craig, K. D. (2012). Empathy and pain. In R. F. Schmidt & G. F. Gebhart (Eds.), *Encyclopedia of Pain, Second Edition.* Heidelberg: Springer- Verlag.

Hadjikhani, N., Zürcher, N. R., Rogier, O., Hippolyte, L., Lemonnier, E., Ruest, T., Ward, N., Lassalle, A., Gillberg, N., Billstedt, E., Helles, A., Gillberg, C., Solomon, P., Prkachin, K. M., & Gillberg, C. (2014). Emotional contagion for pain is intact in autism spectrum disorders. *Translational Psychiatry (e343).* doi: 10.1038/tp.2013.113

Han, S. H., Fan, Y., & Mao, L. (2008). Gender difference in empathy for pain: an electrophysiological investigation. *Brain Research, 1196*, 85-93. doi: 10.1016/jbrainres.2007.12.062

Hamilton, A. F. (2013). Reflecting on the mirror neuron system in autism: A systematic review of current theories. *Developmental Cognitive Neuroscience, 3*, 91-105. doi: 10.1016/j.dcn.2012.09.008

Heberlein, A. S., & Atkinson, A. P. (2009). Neuroscientific evidence for simulation and shared substrates in emotion recognition. *Emotion Review, 1*, 162-177. doi: 10.1177/1754073908100441

Hein, G., & Singer, T. (2008). I feel how you feel but not always: The empathic brain and its modulation. *Current Opinion in Neurobiology, 18*, 153-158. doi: 10.1016/j.conb.2008.07.012

Hynes, C. A., Baird, A. A., & Grafton, S. T. (2006). Differential role of the orbitofrontal lobe in emotional versus cognitive perspective-taking. *Neuropsychologia, 44*, 374-383. doi: 10.1016/j.neuropsychologia.2005.06.011

Jackson, P. L., Meltzoff, A. N., & Decety, J. (2005). How do we perceive the pain of others? A window into the neural processes involved in empathy. *Neuroimage, 24*, 771-779. doi: 10.1016/j.neuroimage.2004.09.006

Keysers, C., Kaas, J. H., & Gazzola, V. (2010). Somatosensation in social perception. *Nature Reviews Neuroscience, 11*, 417-428. doi: 10.1038/nrn2833

Kühn, S., Muller, B. C., van Baaren, R. B., Wietzker, A., Dijksterhuis, A., & Brass, M. (2010). Why do I like you when you behave like me? Neural mechanisms mediating positive consequences of observing someone being imitated. *Social Neuroscience, 5*, 384-392. doi: 10.1080/17470911003633750

Lakin, J. L., & Chartrand, T. L. (2003). Using nonconscious behavioral mimicry to create affiliation and rapport. *Psychological Science, 14*, 334-339. doi: 10.1111/1467-9280.14481

Lakin, J. L., Chartrand, T. L., & Arkin, R. M. (2008). I am too just like you – Nonconscious mimicry as an automatic behavioral response to social exclusion. *Psychological Science, 19*, 816-822. doi: 10.1111/j.1467-9280.2008.02162.x

Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage, 54*, 2492-2502. doi: 10.1016/j.neuroimage.2010.10.014

Lamm, C., Meltzoff, A. N., & Decety, J. (2010). How do we empathize with someone who is not like us? A functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience, 22*, 362-376. doi: 10.1162/jocn.2009.21186

Lamm, C., Nusbaum, H. C., Meltzoff, A. N., & Decety, J. (2007). What are you feeling? Using functional magnetic resonance imaging to assess the modulation of sensory and affective responses during empathy for pain. *PloS One*, *12*: e 1292. doi: 10.1371/journal.pone.0001292

Liepelt, R., von Cramon, D. Y., & Brass, M. (2008). What Is Matched in Direct Matching? Intention Attribution Modulates Motor Priming. *Journal of Experimental Psychology: Human Perception and Performance, 34*, 578-591. doi: 10.1037/0096-1523.34.3.578

Loggia, M. L., Mogil, J. S., & Bushnell, M. C. (2008). Empathy hurts: Compassion for another increases both sensory and affective components of pain perception. *Pain, 136*, 168-176. doi: 10.1016/j.pain.2007.07.017

Schulte-Ruther, M., Markowitsch, H. J., Fink, G. R., & Piefke, M. (2007). Mirron neuron and theory of mind mechanisms involve face-to-face interactions: a functional magnetic resonance imaging approach to empathy. *Journal of Cognitive Neuroscience, 19*, 1354-1372. doi: 10.1162/jocn.2007.19.8.1354

Shamay-Tsoory, S. G., Aharon-Peretz, J., & Perry, D. (2009). Two systems for empathy: a double dissociation between emotional and cognitive empathy in inferior frontal gyrus versus ventromedial prefrontal lesions. *Brain, 132*, 617-627. doi: 10.1093/brain/awn279

Singer, T., & Lamm, C . (2009). The Social Neuroscience of Empathy. *Annals of the New York Academy of Sciences, 1156*, 81-96. doi: 10.1111/j.1749-6632.2009.04418.x

Singer, T., Seymour, B., O' Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for Pain Involves the Affective but not Sensory Components of Pain. *Science, 303,* 1157-1162. doi: 10.1126/science.1093535

Singer, T., Seymour, B., O' Doherty, J. P., Stephan, K. E., Dolan, R. J., & Frith, C. D. (2006). Empathic neural responses are modulated by the perceived fairness of others. *Nature, 439*, 466-469. doi: 10.1038/nature04271

Spengler, S., Bird, G., & Brass, M. (2010). Hyperimitation of actions is related to reduced understanding of others' minds in autism spectrum conditions. *Biological Psychiatry, 15*, 1148-1155. doi: 10.1016/j.biopsych.2010.09.017

Stel, M., van Baaren, R. B., & Vonk, R. (2008). Effects of mimicking: Acting prosocially by being emotionally moved. *European Journal of Social Psychology, 38,* 965-976. doi: 10.1002/ejsp.472

van Baaren, R. B., Holland, R. W., Kawakami, K., & van Knippenberg, A. (2004). Mimicry and Prosocial Behavior. *Psychological Science, 15,* 71-74. doi: 10.1111/j.0963-7214.2004.01501012.x

Völlm, B. A., Taylor, A. N. W., Richardson, P., Corcoran, R., Stirling, J., McKie, S., Deakin, J. F. W., & Elliot, R. (2006). Neural correlates of theory of mind and empathy: a functional magnetic resonance imaging study in a nonverbal task. *Neuroimage, 29,* 90-98. doi: 10.1016/j.neuroimage.2005.07.022

Williams, J. H. G., Whiten, A., & Singh, T. (2004). A systemic review of action imitation in autism spectrum disorder. *Journal of Autism and Developmental Disorders, 34,* 285-299. doi: 10.1023/B:JADD.0000029551.56735.3a

Xu, X. J., Zuo, X. Y., Wang, X. Y., & Han, S. H. (2009). Do you feel my pain? Racial group membership modulates empathic neural responses. *Journal of Neuroscience, 29,* 8525-8529. doi: 10.1523/JNEUROSC.2418-09.2009

Yang, C. Y., Decety, J., Lee, S. Y., Chen, C. Y., & Cheng, Y. W. (2009). Gender differences in the mu rhythm during empathy for pain: An electroencephalographic study. *Brain Research, 1252,* 176-184. doi: 10.1016/j.brainres.2008.11.062